Review of CalEPA/OEHHA Worker Air/Blood Lead Modeling Approach

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Abbreviations

ALM	Adult Lead Model
ALV	Alveolar
BCI	Battery Council International
BMF	Battery Manufacturing Facility
CalEPA	California Environmental Protection Agency
ET	Extrathoracic
GI	Gastrointestinal
GSD	Geometric Standard Deviation
HRTM	Human Respiratory Tract Model
IAF	Inhalability Adjustment Factor
ICRP	International Commission on Radiological Protection
ILA	International Lead Association
IEUBK	Integrated Exposure Uptake Biokinetic
ITC	Inhalation Transfer Coefficient
MMAD	Mass Median Aerodynamic Diameter
MPPD	Multiple-Path Particle Dosimetry
OEHHA	Office of Environmental Health Hazard Assessment
PbA	Air Lead
PbB	Blood Lead
PBPK	Physiologically-Based Pharmacokinetic
PSD	Particle Size Distribution
RIVM	National Institute of Public Health and Environment (Netherlands)
SAB	Science Advisory Board
SSF	Secondary Smelter Facility
TB	Tracheobronchial
US EPA	United States Environmental Protection Agency

Executive Summary

As requested by the International Lead Association (ILA) and the Battery Council International (BCI), Gradient has reviewed the technical approach used by the California Environmental Protection Agency/Office of Environmental Health Hazard Assessment (CalEPA/OEHHA) to evaluate worker lead exposures, as presented in the October 2013 report *Estimating Workplace Air and Worker Blood Lead Concentration using an Updated Physiologically-based Pharmacokinetic (PBPK) Model* (CalEPA, 2013). The OEHHA report presents the modeling methodology the Agency used to estimate blood lead (PbB) concentrations corresponding to specified air lead (PbA) concentrations and provides results that are intended to support efforts to develop workplace standards for lead exposures. This review focuses on several aspects of the OEHHA modeling approach that raise questions regarding the validity of the modeling results and the conclusions drawn based on those results. Additional comments may be prepared regarding the OEHHA approach as the process of evaluating California workplace exposure standards for lead proceeds.

The multi-step modeling approach described in the OEHHA report addresses a number of factors that influence workplace exposures to airborne lead, including the role of particle size in deposition and absorption in the body. The approach includes a model that predicts how particles of varying size distributions will be deposited in different regions of the respiratory tract (*i.e.*, the Multiple-Path Particle Dosimetry [MPPD] Model) and another model that predicts PbB concentrations resulting from assumed lead exposure levels (*i.e.*, the Leggett+ model). The approach also incorporates assumptions regarding factors such as rates of particle clearance from the body, breathing rates, lead absorption rates from various body compartments, and the variability of PbB concentrations in exposed populations.

The analysis presented in this review identified a number of corrections and modifications that are needed to address errors in the modeling approach and strengthen the scientific foundation of the results, including:

- Correcting the application of the MPPD model to include an MPPD model-recommended inhalability adjustment factor (IAF) when evaluating larger particles (*i.e.*, particles with a mass median aerodynamic diameter [MMAD] greater than 5-8 μm);
- Modifying the derivation of the Inhalation Transfer Coefficient (ITC), which estimates the fraction of inhaled airborne lead on particulates that is absorbed in the body, to reflect:
  - Current scientific knowledge regarding the clearance of inhaled/deposited particles from the body, and the timing of particle clearance from the respiratory tract to the gastrointestinal (GI) tract; and
  - Corresponding changes in the duration of various GI conditions that would be encountered by particles transported to the GI tract and the resulting time-weighted average values for lead absorption from the GI tract; and
- Expanding the particle size range considered in the modeling efforts to reflect additional available data, including data recently collected by BCI members at battery manufacturing and secondary smelter facilities.

As illustrated in this review, the current OEHHA model results overestimate the mass of inhaled particulates that will be deposited in the respiratory tract, the fraction of inhaled lead that will be deposited and absorbed into the body, and the resulting PbB concentration for a given PbA exposure. The current approach also led OEHHA to incorrectly conclude that particle size (in the 1-15 μm MMAD size range) does not affect the fraction of lead from airborne particulates that will be transferred to the blood (*i.e.*, following inhalation, deposition, and absorption). Consequently, the model yields inaccurate predictions of the PbB concentrations that would be associated with specific PbA concentrations, and does not provide a sound basis for evaluating potential workplace exposures or standards. As a result, OEHHA should conduct additional modeling, applying the recommended corrections and modifications reflecting the best currently available science. Only by implementing the recommended changes will the revised modeling yield results that more accurately reflect the current state of the science.

1 Introduction

As requested by the International Lead Association (ILA) and the Battery Council International (BCI), Gradient has reviewed the technical approach used by the California Environmental Protection Agency/Office of Environmental Health Hazard Assessment (CalEPA/OEHHA) to evaluate worker lead exposures, as presented in the October 2013 report *Estimating Workplace Air and Worker Blood Lead Concentration using an Updated Physiologically-based Pharmacokinetic (PBPK) Model* (CalEPA, 2013). The OEHHA report presents the modeling methodology the Agency used to estimate blood lead (PbB) concentrations corresponding to specified air lead (PbA) concentrations and provides results that are intended to support efforts to develop workplace standards for lead exposures. This review focuses on several aspects of the OEHHA modeling approach that raise questions regarding the validity of the modeling results and the conclusions drawn based on those results. Additional comments may be prepared regarding the OEHHA approach as the process of evaluating California workplace exposure standards for lead proceeds.

The multi-step modeling approach described in the OEHHA report addresses a number of factors that influence workplace exposures to airborne lead, including the role of particle size in deposition and absorption in the body. The approach includes a model that predicts how particles of varying size distributions will be deposited in different regions of the respiratory tract (*i.e.*, the Multiple-Path Particle Dosimetry [MPPD] model) and another model that predicts PbB concentrations resulting from assumed lead exposure levels (*i.e.*, the Leggett+ model). The approach also incorporates assumptions regarding factors such as rates of particle clearance from the body, breathing rates, lead absorption rates from various body compartments, and the variability of PbB concentrations in exposed populations.

This review focuses on aspects of the modeling approach that significantly influence the model results. The review also identifies the following specific quantitative corrections and modifications to OEHHA's modeling approach:

- Correcting the application of the MPPD model to include an MPPD model-recommended inhalability adjustment factor (IAF) when evaluating larger particles (*i.e.*, particles with a mass median aerodynamic diameter [MMAD] greater than 5-8 μm);
- Modifying the derivation of the Inhalation Transfer Coefficient (ITC), which estimates the fraction of airborne lead from particulates that is absorbed in the body, to reflect:
  - Current scientific knowledge regarding the clearance of inhaled/deposited particles from the body and the timing of particle clearance from the respiratory tract to the gastrointestinal (GI) tract; and
  - Corresponding changes in the duration of various GI conditions that would be encountered by particles transported to the GI tract and the resulting time-weighted average values for lead absorption from the GI tract; and
- Expanding the particle size range considered in the modeling efforts to reflect additional available data, including data recently collected by BCI at battery manufacturing and secondary smelter facilities.

As illustrated in this review, implementing these recommended modifications demonstrates that the current OEHHA approach overestimates the fraction of lead from airborne particles that will be absorbed into the body, particularly for larger particles. As a result, the current OEHHA approach overestimates the PbB concentration predicted to be associated with a specific PbA concentration and underestimates the PbA concentration associated with a specific target PbB concentration. In addition, calculations using the modified approach indicate that a central conclusion of the OEHHA report is not correct, *i.e.*, the modified calculations show that the ITC values differ depending on the assumed particle size distribution of lead exposures (including consideration of particles in the 1-15 μm and greater MMAD size range). To correct these errors and strengthen the scientific foundation for the OEHHA analysis, the recommended changes will increase the reliability of the modeling efforts by correctly applying the selected models, best reflecting current scientific knowledge and available data, and providing a more accurate and technically sound foundation for decision-making regarding occupational exposure limits.

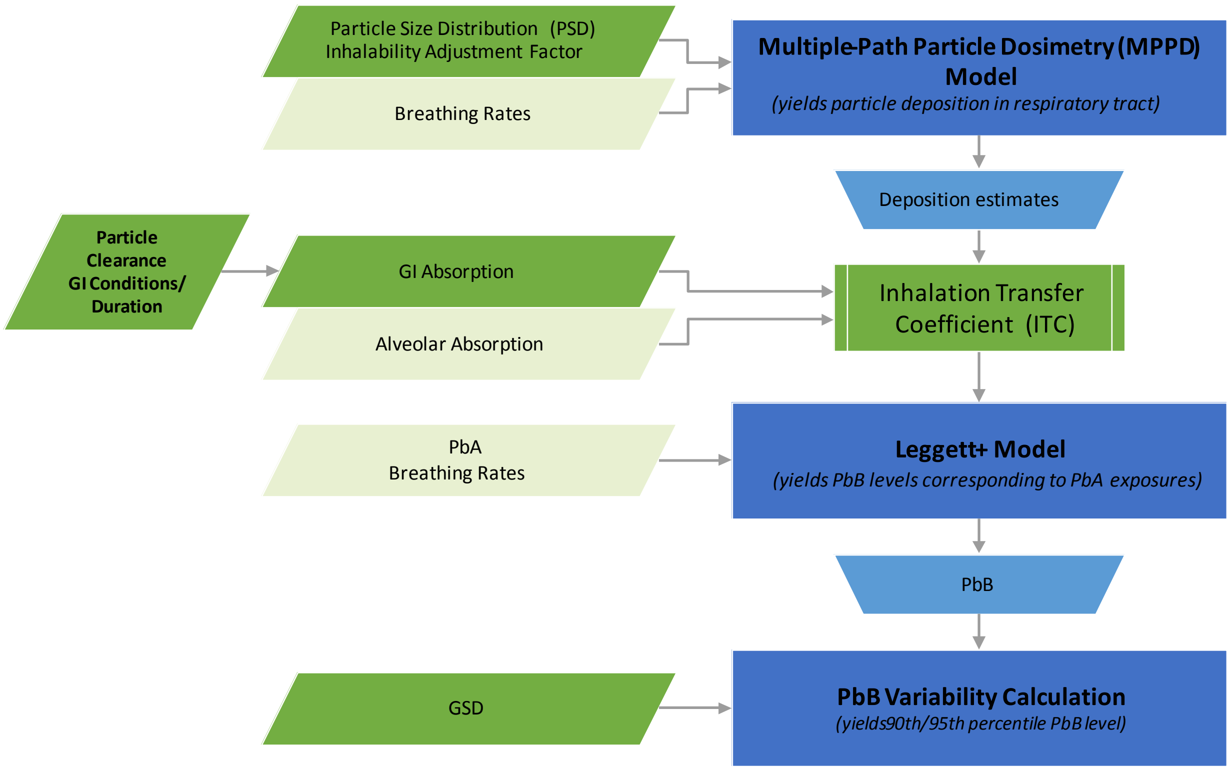
Section 2 of this review briefly summarizes the OEHHA modeling approach, while Section 3 reviews the recommended corrections and modifications, and the basis for these recommendations. Section 4 illustrates the implications of the recommended changes for the modeling results and for evaluating potential occupational exposure limits.

2 Overview of OEHHA Modeling Approach

The OEHHA PBPK report (CalEPA, 2013) describes the modeling approach that the Agency used to estimate PbB concentrations corresponding with workplace PbA concentrations. This modeling approach includes four main steps:

1. Particle deposition in the respiratory tract: Data regarding the particle size distribution of airborne particles, PbA concentrations, and other assumptions (such as breathing patterns and rates) were applied in the MPPD model to estimate the deposition of inhaled particles in three compartments of the respiratory tract.
2. Particle clearance processes and lead absorption: Information regarding clearance of inhaled particles (particularly to the GI tract) was combined with information regarding the timing and extent of lead absorption from the respiratory and GI tracts to estimate the overall percentage of lead from inhaled particles that is transferred to the blood (the ITC).
3. Mean modeled PbB concentrations: Information regarding lead absorption was combined with other exposure assumptions within a PBPK model (the OEHHA-developed Leggett+ model) to develop central tendency estimates of PbB concentrations associated with various PbA concentrations.
4. High-end modeled PbB concentrations: An estimate of worker population variability in PbB concentrations was used to develop high-end estimates of PbB concentrations associated with various PbA concentrations.

The key elements of the OEHHA modeling approach are summarized in Figure 2.1.



Note: GI = gastrointestinal; GSD = geometric standard deviation; PbA = air lead; PbB = blood lead.

Figure 2.1 Overview of CalEPA/OEHHA Lead Modeling Approach

2.1 Particle Deposition

Entry, deposition, and retention of airborne particles in the respiratory tract are dependent on several factors, including exposure concentration and duration, breathing patterns and rates, and particle properties (*i.e.*, size, shape, and chemical composition) (US EPA, 2009a). It is well established that particle size is the major determinant of the fraction of particles that are deposited in and cleared from the various regions of the respiratory tract (Hinds, 1999; US EPA, 2009a). To evaluate particulate deposition, the human respiratory system has generally been divided into three major regions: 1) the extrathoracic (ET) region, which includes the nose, mouth, pharynx, and larynx; 2) the tracheobronchial (TB) region, which includes the region from the trachea to the terminal bronchioles; and 3) the pulmonary or alveolar (ALV) region, which includes the alveoli where gas exchange takes place (Figure 2.2). These three regions of the respiratory tract differ in structure, airflow patterns, function, and the corresponding sizes of particles that penetrate and deposit in each region. A variety of factors influence the mechanisms of particle deposition; together with particle characteristics, these factors determine overall deposition in each region. As discussed further below, the ultimate fate of the particles differs depending on where particles deposit. For example, particles that deposit in the ALV region will be absorbed, while most particles that deposit in the ET and TB regions will be moved toward the trachea, swallowed, and ultimately ingested and subjected to absorption in the GI tract; however, a portion of the particles that deposit in the ET region will be cleared from the body prior to absorption.

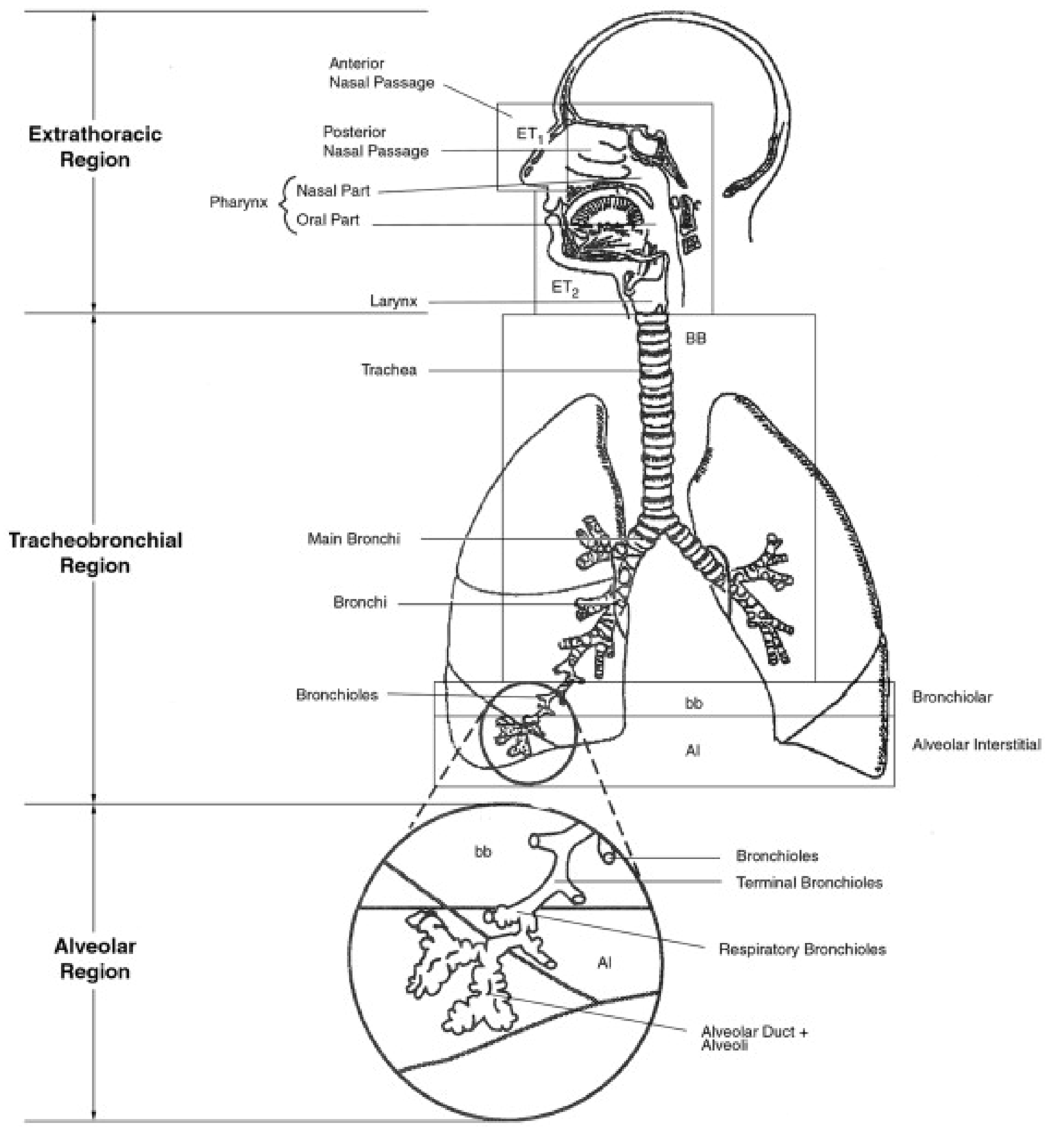


Figure 2.2 Major Regions of the Human Respiratory System. Source: Hofmann, 2011.

Several mathematical models have been developed to predict total and regional deposition of particles in the respiratory system (Rostami, 2009; Hofmann, 2011; Heyder, 2004; Anjilvel and Asgharian, 1995; Asgharian *et al*., 2001). To model particle deposition, OEHHA used the MPPD model, a whole-lung deposition model that incorporates respiratory tract geometry, particle size distribution data, and data on breathing patterns to calculate the fraction of deposited particles in each of the three major regions of the respiratory tract. The model documentation indicates that the model was designed to predict deposition and clearance of particles ranging in size from ultrafine (< 0.01 μm) to coarse (~20 μm); however, larger particle sizes can also be entered in the model (Price, 2014). As the MMAD values increase beyond the identified target model range, a greater degree of uncertainty might be expected; however, model deposition estimates are consistent with researcher observations and predictions of reduced inhalability/deposition efficiency for larger particle sizes.

The MPPD model was first developed by the CIIT Center for Health Research, with support from the National Institute of Public Health and Environment (RIVM) in the Netherlands (Netherlands RIVM, 2002), and was updated in 2006 (v. 2.11).[1] The MPPD model has been used in a variety of contexts, *e.g.*, by the United States Environmental Protection Agency (US EPA, 2009a) to evaluate air quality standards for particulate matter, by other researchers (*e.g.*, Oller and Oberdorster, 2010) to assess human and animal exposures to nickel, and in a comprehensive evaluation of the potential health impacts of occupational exposures to lead, conducted by the lead industry in response to a request from the European Commission (LDAI, 2008). The theoretical basis for the model is described by Anjilvel and Asgharian (1995), with additional details available in Rostami (2009), Hofmann (2011), and Asgharian *et al*. (2001).

In the evaluations presented in its report (CalEPA, 2013), OEHHA relied primarily on particle size distributions and PbA concentration data measured in secondary smelter, radiator, battery manufacturing, and lead powder facilities in Korea (Park and Paik, 2002). Apparently based on the data from this study, OEHHA focused the analyses it presented in its report primarily on particles with an MMAD of up to approximately 15 µm. OEHHA's report also presents analyses reflecting simulations of different activity levels, such as resting, sitting, light work, moderate work, and heavy work, which were obtained by varying inputs to the MPPD model (*i.e.*, breaths/min and tidal volume).

2.2 Particle Clearance/Lead Absorption

As noted above, the fate of lead from particles deposited in the respiratory tract depends on particle clearance and lead absorption processes that vary with regard to their timing and the extent to which they occur (Hofmann, 2011; Rostami, 2009; Smith *et al*., 2011, 2013; US EPA, 2009a). Particles that are deposited in the ALV region are cleared more slowly, and 100% of the lead from particles deposited in this region is assumed to be absorbed into the body. By contrast, particles deposited in the ET and TB region are cleared more rapidly, with most particles being transferred to the GI tract (where the lead is absorbed to a substantially lesser degree than from the ALV region of the respiratory tract). Some portion of the deposited particles is also completely cleared from the body with none of the lead from such particles being absorbed (*e.g.*, particles that are removed from the ET region by nose blowing or wiping). In the OEHHA approach, information regarding particle deposition and lead absorption was combined to yield the ITC, which represents the percentage of the lead on the inhaled particles that was ultimately deposited and absorbed in the body.

In the OEHHA approach, lead from particles that are deposited in the ALV region of the respiratory tract is assumed to be 100% absorbed. By contrast, lead-bearing particles deposited elsewhere in the respiratory tract are assumed to be transported to the GI tract, with lead absorption varying based on the conditions the particle encounters when it reaches the GI tract (*i.e.*, a fed, fasting, or between-meals state). The following equation illustrates the overall ITC calculation used in the OEHHA modeling:

[1] The MPPD model is available for download at http://www.ara.com/products/mppd.htm.

$$ITC = [\%Dep_{ALV} \times Ab_{ALV}] + [\%Dep_{non-ALV} \times Ab_{GI-non-ALV}]$$

where:

$\%Dep_{ALV}$ and $\%Dep_{non\text{-}ALV}$	=	the percent of inhaled particles deposited in the alveolar and other (non-alveolar) regions of the respiratory tract, respectively (as calculated using the MPPD model)
Ab_{ALV}	=	Lead absorption from the alveolar region to the bloodstream (assumed to be 100%)
$Ab_{GI\text{-}non\text{-}ALV}$	=	Lead absorption from the GI tract following particle transport from the non-alveolar regions of the respiratory tract to the GI tract

The calculation applied in the OEHHA modeling approach essentially assumed that particles deposited in the non-alveolar regions of the respiratory tract are transported to the GI tract at a steady rate throughout the day. As a result, the value of $Ab_{GI\text{-}non\text{-}ALV}$ used in the OEHHA calculations is a 24-hour time-weighted average calculated using the following formula:

$$Ab_{GI-24hr} = \frac{[(Ab_{fast} \times D_{fast}) + (Ab_{bet} \times D_{bet}) + (Ab_{fed} \times D_{fed}) + (Ab_{no} \times D_{no})]}{24}$$

where the Ab and D values are the GI absorption, and durations of various GI conditions, as shown in the following table:

GI Condition	GI Absorption (Ab)	Duration (hr/day) (D)
Fasting	50%	10
Between meals	19%	10
Fed	12%	2
No absorption	0%	2

OEHHA identified the GI absorption values based on limited available scientific literature (*i.e.*, nine studies conducted between the late 1960s and the mid-1980s that typically reflect small numbers of subjects exposed to ingested lead under a variety of conditions). OEHHA's duration assumptions are based on professional judgment (with negligible information provided regarding the basis for OEHHA's choices) and yield a time-weighted GI absorption value of 30%. When OEHHA applied this value in the ITC formula for the GI absorption from particles deposited in the non-alveolar regions ($Ab_{GI\text{-}non\text{-}ALV}$), it calculated that the value of the ITC was also 30%. This ITC value plays a critical role in linking the information regarding particle size/deposition/absorption with the PBPK modeling conducted in the next step.

2.3 Blood Lead Modeling

In the next step of its modeling process, OEHHA applied the ITC estimate, together with other exposure assumptions (*e.g.*, breathing rates), within a PBPK model to predict the PbB concentrations that would result from workplace exposure to specific PbA concentrations. Such models integrate information regarding how lead is absorbed, distributed, and eliminated from the body to predict PbB concentrations associated with various exposure conditions. OEHHA evaluated several lead models – focusing primarily on models developed by Bert *et al*. (1989), Leggett (1993), and O'Flaherty (1993, 1995) – and selected the Leggett model for use in its evaluations. OEHHA modified the original Leggett Model to include various aspects of workplace exposure not reflected in the original structure (*e.g.*, use of the ITC) and renamed the resulting modified model as the Leggett+ model. Although OEHHA consulted with a limited number of external scientists while developing the Leggett+ model, the modified model has not been subject to broader scientific peer review.

A primary driver in OEHHA's choice of the Leggett model appears to have been the model's availability in a form that could readily be worked with and modified (*e.g.*, as discussed on pp. 40-42 of the OEHHA report). The relative technical merits of the reviewed models (*e.g.*, with regard to the validity of the PbB predictions generated by each model) were only briefly discussed.

2.4 Population Blood Lead Variability

In the final step of its modeling effort, OEHHA derived high-end estimates (*i.e.*, 90^{th} and 95^{th} percentile values) of PbB concentrations associated with specific PbA concentrations using an estimate of the population variability in PbB concentrations (*i.e.*, the geometric standard deviation [GSD] of the PbB concentrations). The GSD estimate was applied in the standard formula for calculating percentiles in a lognormal distribution; *e.g.*, for the 95^{th} percentile, the following formula was used:

$$\text{PbB } (95^{th} \text{ percentile}) = \text{PbB } (50^{th} \text{ percentile}) \times \text{GSD}^{1.64}$$

Such an approach has been used in other PbB modeling efforts, particularly for analyses supporting development of soil cleanup levels in residential settings, focusing primarily on young children (*e.g.*, Griffin *et al*., 1999; Bowers and Mattuck, 2001). Appropriate estimates of population variability for such calculations are not intended to reflect differences in the exposure conditions or sources under consideration (*e.g.*, when setting soil cleanup levels, differences in the soil lead concentrations to which individuals are exposed). Instead, such variability estimates are intended to reflect various aspects of interindividual- or community-level variability, which can be related to differences in behavior patterns (*e.g.*, soil ingestion rates), biological responses to lead exposure (*e.g.*, absorption), or other exposure sources and pathways (*e.g.*, dietary sources) (*e.g.*, US EPA, 2009b; 2011). As a result, when deriving GSDs for use in PbB modeling, GSDs should be based on data from population groups/subgroups with comparable exposure levels.

OEHHA chose a GSD of 1.6 to estimate the variability in PbB concentrations in lead-exposed worker populations. As described by OEHHA, this value reflects data from the general population, particularly from studies in children in residential settings (Griffin *et al*., 1999; White *et al*., 1998). OEHHA selected this value recognizing the limited appropriate data for determining a GSD for PbB modeling in worker populations. For additional context for its choice, OEHHA also examined GSD values calculated from several older worker PbB studies (Gross, 1979, as cited in CalEPA, 2013, 1981; Griffin *et al*., 1975; Williams *et al*., 1969; and Azar *et al*., 1975). Based on estimated lead intake levels, OEHHA calculated GSDs that were less than (for worker groups estimated to have low or medium lead intake) and greater than (for worker groups estimated to have high lead intake) the GSD of 1.6 used in the calculations. OEHHA used the selected GSD to estimate 90^{th} and 95^{th} percentile PbB concentrations based on the 50^{th} percentile values predicted by the PBPK model.

3 Key Issues with OEHHA's Modeling Approach

This review of the OEHHA modeling report identified a number of issues that raise questions regarding the validity of the quantitative model results and several of OEHHA's conclusions. In particular, OEHHA's conclusion that the ITC does not vary greatly for particle size distributions in the range of 1-15 μm MMAD does not reflect accurate, up-to-date, and complete consideration of the available models and scientific data, and is not supported by the modified analyses presented below. Key corrections and modifications that are needed to strengthen the scientific foundation of the modeling approach are as follows:

- Correcting the MPPD modeling conducted for larger particles (> 5-8 μm) to reflect an adjustment factor built into the model for larger particles;
- Modifying the ITC calculation to reflect updates in the underlying science and models, and corresponding changes in GI absorption assumptions; and
  - Including a more comprehensive range of workplace particle sizes (particularly particles with MMAD values > 15 μm) in the modeling scenarios.

The following sections focus on these key issues with OEHHA's modeling approach and assumptions and present recommendations for quantitative corrections and modifications to the modeling approach. These sections also briefly discuss other efforts that should be undertaken to better document and justify certain modeling choices (*e.g.*, regarding particle size data, GI absorption, GSD values, and model validation) and to better assess the consistency of the model results with workplace observations, before regulatory conclusions are based upon these results.

3.1 Correction to MPPD Modeling for Larger Particles (Use of an Inhalability Adjustment Factor)

OEHHA used the MPPD model to estimate deposition of lead-containing particles of various sizes within three major regions of the respiratory tract. The MPPD model includes an IAF, which the model documentation indicates is to be applied when modeling deposition of particles with an MMAD >8 μm (and model developers indicate may be appropriate for particles >5 μm; Price, 2014). This factor accounts for the fact that the data underlying the MPPD model development primarily reflect studies of smaller particles (generally < 10 μm) and also reflect different air flow conditions (*i.e.*, higher wind speeds) than would typically be encountered in indoor workplaces. The IAF is intended to account for available data indicating that larger particles encountered in indoor environments will not be inhaled and deposited in the respiratory tract to the same extent as predicted by the unadjusted MPPD model (Brown, 2005; Asgharian *et al*., 2001; Menache *et al*. (2005).

However, the results presented in the OEHHA report do not indicate that OEHHA used the IAF in its modeling, even when modeling larger particle size categories (*e.g.*, data from the Park and Paik [2002] study for battery manufacturers [MMAD = 14.1 μm] or lead powder [MMAD = 15.1 μm]). This omission has important impacts on the model predictions. As illustrated by the analyses summarized in Table 3.1 and Figure 3.1, if the IAF is omitted from the modeling calculations for larger particle size categories, the overall percentage of inhaled particles calculated to be deposited in the respiratory tract is greater than the percentage that is calculated when correctly applying the IAF. As a result, the amount of absorbed lead will also be overestimated, and the PbB concentration estimated to correspond to a specific PbA concentration will also be greater. As shown in Table 3.1 and Figure 3.1, the difference between the deposition calculated to occur with *vs*. without the IAF is greater for larger particle sizes (*i.e.*, the degree to which lead absorption will likely be overestimated increases as particle size increases).

Table 3.1 Impact of Use of the Inhalability Adjustment Factor on Particle Deposition Estimates from the Multiple-Path Particle Dosimetry Model[2]

MMAD (μm)	Particle Deposition (%)			
	Total Respiratory Tract		ET Region	
	w/IAF	w/o IAF	w/IAF	w/o IAF
8	72	92	65	85
10	66	94	60	88
15	55	96	52	92
20	51	97	48	95

Note:
MMAD =mass median aerodynamic diameter; ET = extrathoracic; IAF = Inhalability Adjustment Factor.

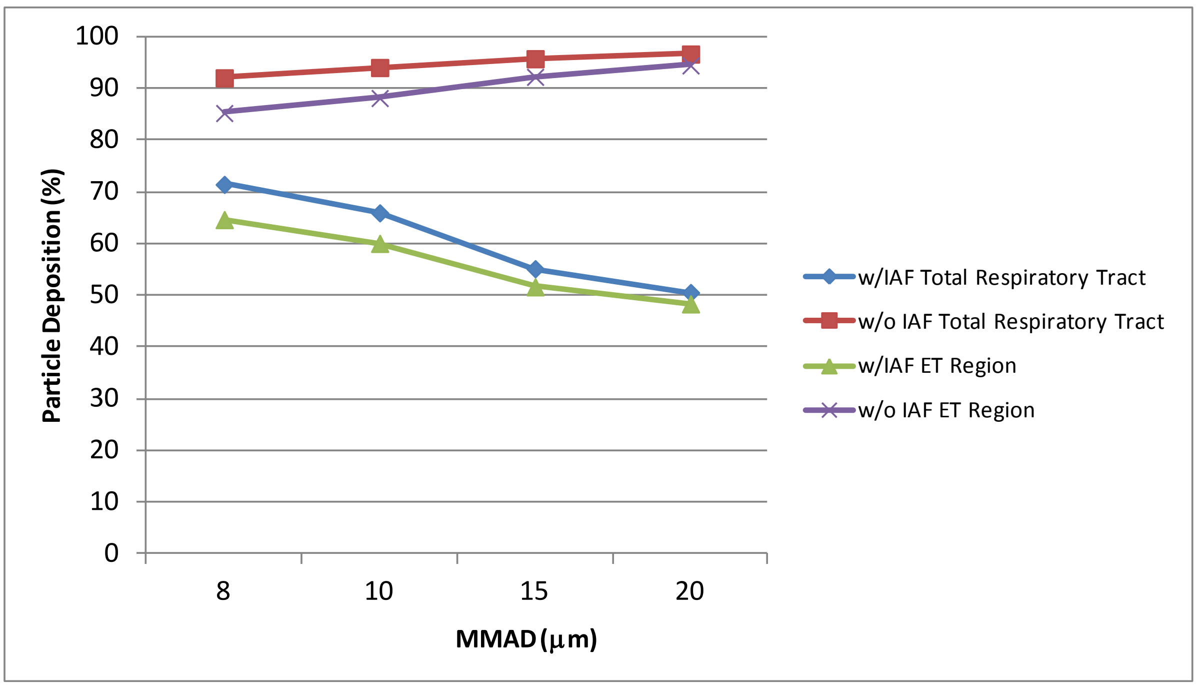


Figure 3.1 Summary of Inhalability Adjustment Factor Impacts on Particle Deposition Estimates From the Multiple-Path Particle Dosimetry Model (model assumptions are same as indicated for results in Table 3.1.)

The MPPD model documentation specifies that this necessary correction should be made to the OEHHA modeling approach (Netherlands RIVM, 2002, 2006). Specifically, the MPPD model documentation

[2] Table shows MPPD model results using a GSD of 4 μm, the Yeh-Schum 5-lobe model, and assuming a unit density particle (0.01 μg/m^3), 20 breaths/min, tidal volume of 1042 mL, and oronasal augmenter breathing pattern.

states that "This adjustment is relevant for particle sizes…larger than about 8 microns for humans; the probability that particles larger than these are inhaled is less than 1.0 and decreases with increasing particle size. This attenuation occurs because of inertial effects." The model developers have indicated that it may also be appropriate to use this adjustment factor for smaller particles (*i.e.*, particles >5 µm) (Price, 2014).

It is also noted that inconsistencies are evident between some of the MPPD modeling results reported by OEHHA for larger particle sizes and observations of likely particle deposition patterns by other researchers. For example, in his paper describing the basis for the Leggett model, Leggett (1993) observed that "A value [for retention of inhaled particles in the lungs] of about 0.35-0.40 may be a reasonable central estimate, but deposition fractions as low as 0.15 or as high as 0.75 may not be uncommon." By contrast, some of the MPPD modeling results provided by OEHHA suggested that approximately 100% of the inhaled particles (*i.e.*, a deposition fraction of 1.0) would be deposited in the respiratory tract, exceeding the central (0.35-0.4) and high end (0.75) deposition fraction estimates suggested by Leggett. As one example, OEHHA's MPPD modeling efforts for battery manufacturing workers at rest (reflecting a larger particle size but excluding the IAF) suggested that 97% of the particles would be deposited in the ET region, 2% would be deposited in the TB region, and 0.6% would be deposited in the ALV region (yielding a total deposition fraction of 0.996).

3.2 Modifications to Inhalation Transfer Coefficient Calculation

The ITC is used to estimate lead absorption from inhaled airborne particles, taking into account particle deposition and clearance from various regions of the respiratory tract and differences in lead absorption in different parts of the body. Based on the review reflected in this report, two aspects of the ITC calculation need to be modified to better reflect current scientific knowledge and modeling approaches:

- The patterns of particle clearance (to reflect the existence of rapid and slow phases of clearance to the GI tract, as well as clearance to the external environment) and differences in such patterns for different respiratory tract regions), and
- Differences in GI absorption corresponding to these different clearance patterns.

As described in Section 2.2, OEHHA's assumptions yielded a time-weighted GI absorption value of 30%. When OEHHA applied this value in the ITC formula for the GI absorption from particles deposited in the non-alveolar regions ($Ab_{GI\text{-}non\text{-}ALV}$), it calculated that the value of the ITC was also 30%.

3.2.1 Modifications to Particle Clearance Assumptions

A number of studies and other information sources (discussed below) indicate that particle clearance from the non-alveolar regions of the respiratory tract (*i.e.*, the ET and TB regions) does not occur at a single steady rate (as assumed by OEHHA and discussed in Section 2.2), but instead is a complex process with a number of phases and with differing rates estimated for various respiratory tract compartments. Moreover, available scientific data indicate that some of the particles deposited in the ET compartment of the respiratory tract are cleared from the body to the external environment as a result of nose blowing and other similar processes. Thus, such particles are not transferred to the GI tract, and the lead from such particles is not absorbed into the body.

To more accurately reflect these processes, the estimate of the percentage of inhaled particles deposited in the non-alveolar regions of the respiratory tract applied in the ITC formula presented in Section 2.2 ($\%Dep_{non\text{-}ALV}$) should be revised as follows:[3]

- The two components of the total percentage of particles deposited in the non-alveolar regions (*i.e.*, the percentage of particles deposited in the ET region [$\%Dep_{ET}$] and in the TB region [$\%Dep_{TB}$]) should be addressed separately rather than as a combined value (*i.e.*, the parameter $\%Dep_{non\text{-}ALV}$ used in OEHHA's formula).
- The percentage of the particles deposited in the ET region (as derived using the MPPD model) should be apportioned into three categories, *i.e.*, a fraction of particles that is cleared from the body to the external environment ($Clr_{ET\text{-}ext}$), a fraction that is rapidly cleared to the GI tract ($Clr_{ET\text{-}rapid}$), and one that is slowly cleared to the GI tract ($Clr_{ET\text{-}slow}$).
- The percentage of the particles deposited in the TB region (as derived using the MPPD model) should also be apportioned between a fraction that is rapidly cleared and one that is more slowly cleared to the GI tract (using $Clr_{TB\text{-}rapid}$ and $Clr_{TB\text{-}slow}$).

A conceptual illustration of OEHHA's ITC calculation is shown in Figure 3.2, while the proposed modifications to the ITC calculation are illustrated conceptually in Figure 3.3.

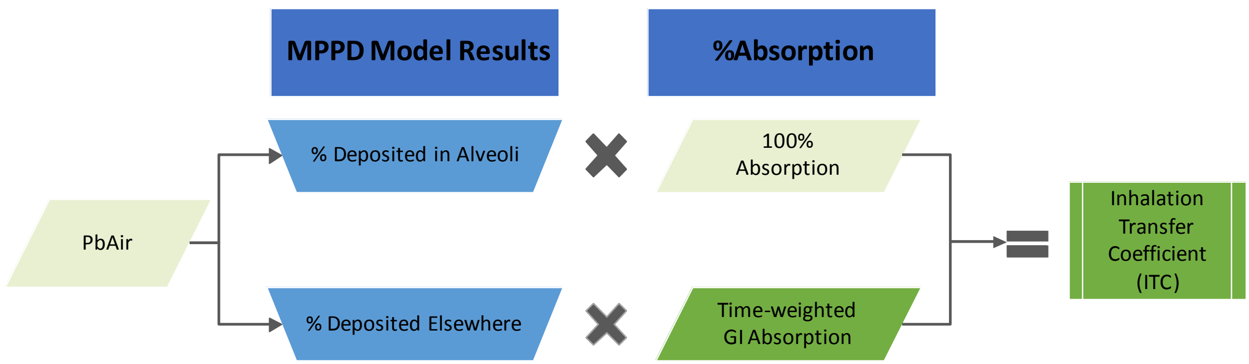


Figure 3.2 Overview of OEHHA Gastrointestinal Absorption/Inhalation Transfer Coefficient Calculations

[3] The parameter abbreviations defined in these bullets (*e.g.*, $\%Dep_{ET}$) are applied in the equation presented in the discussion following Figure 3.3.

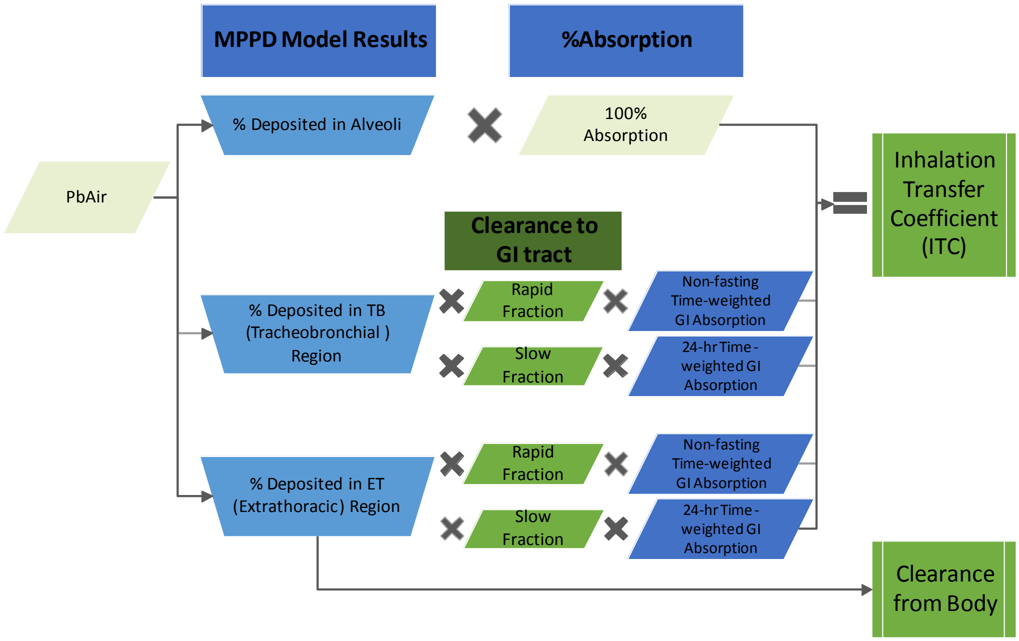


Figure 3.3 Overview of Modified Gastrointestinal Absorption/Inhalation Transfer Coefficient Calculations

Applying these changes alters the non-alveolar portion of the OEHHA formula presented above for calculating the ITC. Specifically, the following formula was used by OEHHA:

$$ITC = [\%Dep_{ALV} \times Ab_{ALV}] + [\%Dep_{non-ALV} \times Ab_{GI-non-ALV}]$$

while the following equation reflects the recommended modifications:

$$ITC = [\%Dep_{ALV} \times Ab_{ALV}]$$

$$+ [\%Dep_{ET} \times Clr_{ET-rapid} \times Ab_{ET-rapid}] + [\%Dep_{ET} \times Clr_{ET-slow} \times Ab_{ET-slow}]$$

$$+ [\%Dep_{TB} \times Clr_{TB-rapid} \times Ab_{TB-rapid}] + [\%Dep_{TB} \times Clr_{TB-slow} \times Ab_{TB-slow}]$$

No modifications are proposed for the assumptions for the alveolar portion of the modified equation (*i.e.*, the first line of the modified equation); as in the original equation, it is assumed that 100% of the lead deposited in the alveolar region will be absorbed. Recommended values for the other elements of this equation, and the basis for the proposed values, are described below. Because none of the lead associated with particles that are cleared from the body (*i.e.*, $\%Clr_{ext}$) is absorbed, such particles do not contribute to the ITC calculation and are not included in this equation.

Recommended values for the clearance parameters that should be included in the modified calculations (*i.e.*, $Clr_{ET\text{-}rapid}$, $Clr_{ET\text{-}slow}$, $Clr_{TB\text{-}rapid}$, and $Clr_{TB\text{-}slow}$, as well as Clr_{ext}) are based on several lines of evidence, including information in the scientific literature as described below. The underlying scientific literature provides information and rates for different modes of particle clearance to the GI tract (including some processes that occur within a time frame of minutes after inhalation and others that occur over longer time frames). However, the primary focus in identifying recommended clearance parameters for the above modified calculation was to determine a conservative (*i.e.*, health-protective) estimate of the degree of clearance that would occur prior to the existence of fasting conditions in the GI tract (assumed to begin a number of hours after the completion of the work day exposures and the final food intake of the day, and to persist during the sleeping period). This focus was selected because, in the OEHHA approach, fasting conditions are assumed to yield lead absorption that is substantially greater than absorption under other GI conditions (*i.e.*, the 50% GI absorption OEHHA assumed for fasting conditions is 2.5 times that for between-meal conditions [19%] and more than 4 times that for fed conditions [12%]). Thus, in deriving these recommended modifications, values were extracted from the scientific literature reflecting the approximate percentages of inhaled particles that would be cleared to the GI tract on the order of hours ("rapid" clearance) *vs*. the percentage that would be cleared over a substantially greater time frame ("slow" clearance).

Values for the percentages of deposited particles assigned to the clearance parameter categories are summarized in the following table. The basis for these recommended modifications to the OEHHA ITC calculation approach is summarized below. Additional discussion of corresponding modifications to assumptions regarding GI absorption conditions is provided in Section 3.2.2 of this review.

Table 3.2 Summary of Recommended Particle Clearance Assumptions for Extrathoracic and Tracheobronchial Regions (for use in modified Inhalation Transfer Coefficient equation)

Lung Region of Particle Deposition	% of Deposited Particles Cleared from Body ($\%Clr_{ext}$)	% of Deposited Particles Cleared to GI Tract ($\%Clr_{ET}$ and $\%Clr_{TB}$)	
		Rapid	Slow
Data for all particle sizes			
ET	19	36	45
TB	NA	40	60
Data for larger particles only			
ET	13	62	25
TB	NA	75	25

Notes:
GI = gastrointestinal; ET = extrathoracic; TB = tracheobronchial; NA = not applicable.
Basis for recommended values provided in the following text.

The values presented in Table 3.2 are based on a number of lines of evidence including:

- Scientific research and consequent changes in progress to the ICRP model: The Human Respiratory Tract Model (HRTM) for Radiological Protection developed by a Task Group of the International Commission on Radiological Protection (ICRP) forms an important foundation for inhalation exposure modeling efforts, including elements of the Leggett+ model used by OEHHA to model lead exposures (Leggett, 1993; CalEPA, 2013). As recognized in the OEHHA report, the ICRP model documentation (ICRP, 1994) has served as a "key reference work in this area for nearly 20 years" (CalEPA, 2013). The ICRP model was specifically developed to predict deposition and dose to organs and tissues for male and female adults and children from inhalation of radioactive particles and has been developed and validated based on an extensive body of literature. Although initially published in 1994 (ICRP, 1994), recent modifications have been developed and adopted by ICRP for inclusion in the model (Smith *et al*., 2013). These changes are based in part on data collected in a human volunteer study (Smith *et al*., 2011), in which researchers evaluated the retention of particles in the ET region in a group of nine volunteers exposed to particles of various sizes (*i.e.*, 1.5, 3, and 6 μm), both at rest and while performing light exercise. The authors determined that, on average, approximately 20% of particles were cleared *via* nose blowing. Data summarized in Smith *et al*. (2013; *e.g.*, Table 3) showed that the fraction of deposited particles cleared by mucociliary action was greater, and the time for 50% of such clearance to occur was shorter, for experiments using larger particles (up to 6 μm) and with exercise (relative to results for smaller particles or for resting conditions). These new data have resulted in changes to the ET component of the ICRP model that better address the timing of particle clearance from this respiratory tract region as well as deposited particle clearance from the body *via* nose blowing and similar processes. The recommended values for particle clearance from the ET region listed in Table 3.2 are drawn from this research and the resulting changes to the ICRP model (*e.g.*, Tables 3 and 4 of Smith *et al*., 2011, and Table 1 of Smith *et al*., 2013).

In his comments on OEHHA's modeling efforts (Ginsberg, 2012), Dr. Gary Ginsberg (one of OEHHA's external scientific reviewers) noted that the model included "no accounting for loss of deposited material by coughing, sneezing, and nasal discharge." Although the OEHHA report specifically acknowledges the study conducted by Smith *et al*. (2011) and the role of nose blowing in particle clearance, the Agency states that it "made no attempt to address nose blowing as a pathway for clearing particles from the head region".

- Information regarding clearance processes and timing for the TB region is more sparse; however, ICRP (1994) documentation cites studies indicating that the slow clearance fraction for larger particles (*i.e.*, 6 μm) is approximately 25%, while the fraction for smaller particles is approximately 60% (Stahlhofen and Scheuch, 1990, as cited in ICRP, 1994). The recommended values for particle clearance from the TB region listed in Table 3.2 reflect these findings. In the calculations conducted to support the analyses presented in this review, the fraction of particles deposited in the TB region estimated by the MPPD model was generally relatively small, particularly relative to deposition in the ET region (*i.e.*, generally on the order of single digit percentages). A similar relationship among the estimated deposition fractions is reflected in the modeling analysis results included in the OEHHA report (*e.g.*, Tables B-2 and B-3 of CalEPA, 2013). As a result, assumptions regarding the percentages of these particles that undergo rapid *vs*. slow clearance have a correspondingly smaller influence on the overall ITC calculation.

- Comments from an OEHHA external scientific reviewer regarding modeling approach: Dr. Richard Leggett is one of OEHHA's external scientific reviewers for its modeling approach and is the original developer of the Leggett model that provides one of the crucial foundations for OEHHA's lead modeling efforts. In his peer review (Leggett, 2012), Dr. Leggett noted that the OEHHA modeling was likely to be overestimating the degree to which inhaled particles would be transferred to the GI tract during fasting conditions, stating that "the preponderance of the respiratory deposition of Pb during an 8-hour work day that will eventually be swallowed is likely to be swallowed before the next fasting period begins." Based on modeling efforts reflecting the adopted changes to the ICRP model, he estimated that approximately 80-85% of the inhaled particulate lead would reach the GI tract outside of the time of fasting conditions. His calculation suggests that a greater percentage of particles could be assigned to the rapidly cleared fraction than what is presented in Table 3.2. Such a modification would further reduce the proportion of inhaled/deposited particles that are assumed to be subjected to GI absorption under fasting conditions, and thus would further reduce the predicted degree of lead absorption.

  Dr. Leggett also noted the role of nose blowing and similar processes for particle removal and stated that the modeling he conducted based on the revised ICRP model "predicts that more than 20% of the Pb deposited in the respiratory tract is removed to the environment" *via* such processes. Again, this statement suggests that the values presented above for $\%Clr_{ext}$ represent a conservative (*i.e.*, health-protective) estimate of the proportion of deposited particles that would be subjected to such clearance processes, particularly for larger particles. That is, Dr. Leggett's statements suggest that the recommended values presented in Table 3.2 are likely to overestimate lead absorption, and thus would overestimate the PbB concentration predicted to be associated with a specific PbA concentration.

- Other studies in the scientific literature: Other scientific studies provide additional support for the recommended modifications. General support for the existence of rapid and slow clearance fractions is discussed in a review by Hofmann (2011). Smith *et al*. (2013) reported observations from studies indicating that a fraction of approximately 50% of the particles deposited in the ET region would be cleared within 4-5 hours after exposure (Lippmann, 1970, and Fry and Black, 1973, both as cited in Smith *et al*., 2013). Similarly, Smith *et al*. (2011) reported results from several studies that observed removal by nose blowing and similar removal processes of approximately 15-20% of particles deposited in the ET region (Hounam, 1975, and Hounam *et al*., 1983, both as cited in Smith *et al*., 2011).
- Results from MPPD model using clearance module: Gradient undertook exploratory calculations using the clearance module of the MPPD model and assumptions used by OEHHA to model exposures for battery workers at rest (*e.g.*, exposures during 6 hours of an 8-hour work day). (As discussed above, the OEHHA calculations did not include consideration of clearance of deposited particles to the external environment *via* processes such as nose blowing.) The clearance module is based on data regarding average mucous velocities reflected in the ICRP model (ICRP, 1994). These analyses indicated that a substantial proportion of the deposited particles would be rapidly cleared to the GI tract (*e.g.*, approximately 40% within 7 hours), and also suggested that some of the slowly cleared particles might not be cleared to the GI tract until after the beginning of the following food consumption/work day cycle. (It is noted that the current version of the MPPD model does not reflect the recent changes to the ICRP modeling approach to account for rapid clearance processes; thus, these analyses based on the current MPPD model are likely to underestimate the fraction of deposited particles that would be rapidly cleared to the GI tract.) These two factors would tend to reduce the proportion of the deposited particles that would encounter fasting GI conditions.

Because these updates regarding particle clearance patterns are not included in the current OEHHA modeling approach, the OEHHA approach overestimates the proportion of the deposited particles that will be subjected to the most aggressive, fasting GI absorption conditions. Consequently, the model also overestimates lead absorption – and the corresponding PbB concentration – for specific PbA concentrations.

3.2.2 Modifications to GI Absorption Approach

As described in the preceding section, the modified clearance approach and other supporting information indicate that a substantial portion of the particles that are deposited in the respiratory tract will be cleared to the GI tract within the rapid clearance phase. As a result of this shorter clearance time, these particles are likely to reach the GI tract during or shortly after the work day and are unlikely to reach the GI tract during fasting conditions. By contrast, the transport of particles subjected to slow clearance processes is likely to be more similar to the process assumed in the OEHHA approach (*i.e.*, a process that is occurring throughout the day). To account for the differences in particle timing in reaching the GI tract for these two distinct phases, two separate GI absorption estimates are needed.

For the rapidly cleared particles, the time-weighted adjustment factor should be calculated using the following modified version of the OEHHA formula that was shown in Section 2.2:

$$Ab_{GI-rapid} = \frac{\left[(Ab_{bet} \times D_{bet}) + \left(Ab_{fed} \times D_{fed}\right)\right]}{14}$$

and using the Ab (GI absorption) and D (duration of various GI conditions) values shown in the following table:

GI Condition	GI Absorption (Ab)	Duration (hr/day) (D)
Between meals	19%	10
Fed	12%	4

This formula, and the associated parameter values, reflect the following modifications from the original formula:

- The component of the original formula addressing the fasting state ($Ab_{fast} \times D_{fast}$) is omitted because the available information regarding the rapid clearance phase indicates that it is unlikely that the rapidly cleared particles would encounter fasting conditions in the GI tract to any significant extent.
- The component of the original formula addressing the "no absorption" state ($Ab_{no} \times D_{no}$) is omitted because OEHHA did not provide any basis for this element of the formula in its report, and no support for such an assumption was identified in the scientific literature or based on exploratory results from the clearance phase of the MPPD model. Thus, the value of D_{no} effectively should be set at 0 hours.
- The duration of the fed state (D_{fed}) is increased from 2 hours per day (in the original formula) to 4 hours per day based on information in the scientific literature indicating that the impact of food intake on reducing lead absorption persists for up to several hours after food intake. For example, James *et al*. (1985), one of the studies reviewed by OEHHA, reported that the influence of meals on lead uptake persisted for up to 3 hours after food consumption. Assuming a food impact of approximately 1.5-2 hours/meal or snack, and the potential for multiple meals or snacks during the day, the assumed 4 hours of "fed" state absorption conditions reflects a reasonably conservative estimate for this parameter. By contrast, the OEHHA assumption of 2 hours/day of fed conditions per 24-hour day is likely to underestimate the duration of such conditions for most individuals.

The assumption that rapidly cleared inhaled particles have a low likelihood of encountering fasting GI conditions also includes consideration of the likely timing of food intake relative to a typical work day. In particular, GI conditions during the work day and for a number of hours after the work day are most likely to reflect "fed" and "between-meal" conditions as a result of typical meal and/or snack intake patterns. By contrast, "fasting" conditions are most likely to occur well after the completion of the work day (and inhalation exposures) – particularly during sleep.

Assuming 10 hours of between-meal GI absorption conditions, 4 hours of "fed" state conditions (for a total of 14 hours), and the corresponding GI absorption values listed in the table above, the time-weighted GI absorption value for rapidly cleared particles is calculated to be 17%.

These modifications are based on the scientific literature and other support described above for quantifying the impacts of the rapid and slow clearance processes. In addition, as noted above, these modifications considered professional judgment regarding the likely distribution of fed, fasting, and between-meal states relative to the timing of workplace exposures.

For the slowly cleared particles, the time-weighted GI absorption value ($Ab_{GI\text{-}slow}$) is calculated using essentially the same formula as used in the OEHHA calculation, with the following exceptions: the values of D_{no} and D_{fed} were changed to 0 hours/day and 4 hours/day, respectively, as described above.

Using these assumptions, the time-weighted GI absorption value for slowly cleared particles is calculated to be 31%.

As discussed in Section 4 of this review, when combined with other recommended modifications to the OEHHA modeling approach, these modified GI absorption values yield ITC values that are less than the value derived by OEHHA (30%) and that vary depending on particle size. Key elements of the OEHHA and modified clearance/absorption approaches are compared in Table 3.3.

Table 3.3 Comparison of Key Elements of Clearance/Absorption Approach

	OEHHA Approach	Modified Approach
Clearance to External Environment (*e.g.*, *via* nose blowing)	Not included	≈15-20% of particles deposited in ET region[a]
Clearance to GI Tract	Essentially steady-state process throughout 24-hour day	Rapidly and slowly cleared fractions[a]
GI Absorption	30% (24-hour time-weighted value)	17% (rapidly cleared fraction) 31% (slowly cleared fraction) (*reflecting differing role of fasting period in absorption*)[b]
Fed State Duration	2 hours/day	4 hours/day (*to reflect greater influence of meals on absorption*)[c]

Notes:

ET = Extrathoracic; GI = gastrointestinal; ICRP = International Commission on Radiological Protection; OEHHA = Office of Environmental Health Hazard Assessment.

(a) Derived primarily from documentation of changes to the ICRP respiratory tract model (as documented in Smith *et al*., 2011, 2013, as well as Hoffman, 2011, Leggett, 2012 , and Ginsberg, 2012).

(b) Re-calculated to correspond with changes in the assumed patterns of particle clearance.

(c) Reflecting information in James *et al*. (1985).

It is noted that the original OEHHA GI absorption assumptions (*i.e.*, 30% as a 24-hour average and 12-50% for various GI conditions), as well as the two modified GI absorption assumptions described above for rapidly-cleared (17%) and slowly-cleared (31%) deposited particles, are generally significantly greater than the value (8%) used in the development of the prior lead workplace standard as well as in other lead assessments and models (*e.g.*, the O'Flaherty lead model, which has been used in a variety of lead exposure evaluation contexts). Most of the GI absorption values are also greater than the default value of 15% for the Leggett model. The assumption of 8% GI absorption of ingested lead applied for adults in the O'Flaherty model reflects consideration of the substantial reductions in GI absorption that occur between birth (when GI absorption of lead is estimated to be approximately 58%) and the age of approximately 8 years old and above (where absorption is estimated to be approximately 8%) (O'Flaherty, 1997). Studies reflecting both fed and fasted conditions were cited in the documentation for the O'Flaherty model assumption (O'Flaherty, 1993), *i.e.*, Rabinowitz *et al*. (1980), Chamberlain *et al*. (1978), and Watson *et al*. (1986). The studies by Rabinowitz *et al*. (1980) and Chamberlain *et al*. (1978) were also considered by OEHHA in its calculations, together with an additional seven studies. The original OEHHA GI absorption values played an important role in OEHHA's assumed ITC of 30% and its conclusion that particle size distributions between 1 and 15 μm do not significantly impact the ITC value. The substantial variation of the OEHHA assumptions from previous assumptions regarding GI absorption and the limitations in the scientific foundation for the OEHHA assumptions argue for care in applying these assumptions and interpreting the results of analyses using these assumptions. Specifically, assuming a GI absorption rate of 30% increases the potential contributions of particles deposited in the ET and TB regions of the respiratory tract to overall lead exposures and subsequent impacts on blood lead levels. Therefore, application of such an approach must take special care to 1) accurately characterize particle size and mass distributions for representative exposure conditions, 2) account for the transport timing and ultimate fate of such particles, and 3) consider the impact of particle size and density on model estimates for particle deposition within the various regions of the respiratory tract.

3.3 Consideration of Expanded Particle Size Range

To model particle deposition using the MPPD model, OEHHA relied primarily on data reported by Park and Paik (2002) of particle size distributions (PSDs) and PbA concentrations from measurements of 117 workers in the secondary smelter (2 facilities), radiator (3 facilities), battery manufacturing (4 facilities), and lead powder production (3 facilities) industries in Korea. The PSDs ranged from 1.3-15.1 µm MMAD. The authors noted a significant difference across industries in average particle sizes and in the fraction of particles in the respirable range (as defined by both the Occupational Safety and Health Administration and the American Conference of Industrial Hygienists).

OEHHA did not explain its rationale for using the study by Park and Paik (2002) as the primary basis for the particle size distributions (MMAD and GSD) that were used to generate absorption estimates. OEHHA also conducted only limited analyses of data from two other studies (Liu *et al*., 1996, Spear *et al*., 1998). It is unclear how these data were considered in the overall analysis, and OEHHA did not show data for the deposition analyses from Spear *et al*. (1998). The OEHHA report also did not appear to reflect incorporation of data from other studies of specific industries within its modeling effort, even when such studies were mentioned in the report (*e.g.*, Hodgkins *et al*., 1991 for battery manufacturing facilities [BMFs]).

Data have also been collected recently by BCI members at nine BMFs and five secondary smelter facilities (SSFs) (Petito Boyce *et al*., 2017). One important finding from this study highlights the significance of sampling method on determining representative particle size distributions and mass concentrations. Specifically, PbA concentrations reported by Petito-Boyce *et al*. (2017) illustrate in particle collection effectiveness and the availability of correction factors for the cascade impactor, but not the cassette sampler. Cassette samplers are demonstrably less effective in collecting larger particle sizes, as previously discussed in a number of studies (Spear *et al*., 1998; Rubow *et al*., 1987; Buchan *et al*., 1986; Davies *et al*., 1999; Spear *et al*., 1997; Stefaniak *et al*., 2009; Teikari *et al*., 2003 Petito Boyce *et al*., 2017). This reduced effectiveness is of particular importance when evaluating data for airborne particulates consisting predominantly of larger-sized particles. It is important to note that additional factors including sampling position for the sampler inlet and the jet flow velocity may also yield different PbA concentration results between cassette and cascade impactor sample data (Huang and Tsai 2001).

Furthermore, particle size distribution data reported in the BCI study indicate that the Park and Paik (2002) data used by OEHHA in its modeling do not adequately represent airborne particle exposures for lead workers in these industries in the US. For example, Park and Paik (2002) reported an average MMAD of 14.1 µm for four BMFs, whereas the analysis of the BCI BMF data yielded average MMADs ranging from 21 to 32 µm for the three job categories evaluated in the study. In addition, Hodgkins *et al.* (1991) reported a range of particle sizes by job in two facilities in the US of 11 to 23 µm. A greater contrast was seen in the data for the SSFs, where Park and Paik (2002) reported an average MMAD of 4.9 µm, based on a limited number of samples (*i.e.*, six samples collected at two SSFs), whereas the analysis of the BCI SSF data (representing 68 samples collected at five facilities) yielded average MMADs for the five job categories evaluated in the study ranging from 15 to 25 µm (Petito Boyce *et al*., 2017). A comparison of sampling approaches and results from published studies and the BCI study are summarized in Table 3.4 below.

Table 3.4 Comparison of Published Data with BCI Study Results (2002, adapted from Petito Boyce *et al.*, 2017)

Job Site	Study	Approaches	Data Analysis	Results	Comparison with Petito-Boyce (2017)
Battery Manufacturing Facilities	Hodgkins *et al.* (1991)	8-stage Marple cascade impactor samplers 2 US facilities (40 samples)	No effectiveness corrections	MMAD (pasting): 23 and 13 µm MMAD (stacking and cast-on-strap): 12-18 µm	BCI avg. MMAD (pasting): 24 µm BCI avg. (assembly): 21 µm
	Liu *et al.* (1996)	4- to 8-stage Marple cascade impactor samplers 1 US facility (44 samples)	MMADs not reported Collected "loose" particles when disassembling samplers	Avg. lead mass for particles >10 µm: ~71-79% Avg. lead mass for particles <1 µm: 0.6-3.4%	BCI avg. lead mass for particles > 10 µm for predominant pattern of BCI samples: ~60-70% (including non-detect results) BCI ag. lead mass for particles <1 µm: 1.4-3.3%
	Park and Paik (2002)	8-stage Marple cascade impactor samplers 4 Korean facilities (44 samples)	Results blank- and efficient-corrected	Avg. MMAD (GSD): 14.5 µm (1.5) Avg. lead mass for particles <1 µm: ~5.0%	Avg. MMAD (GSD): 21-32 µm (~2.5-7) Avg. lead mass for particles <1 µm: ~1.4-3.3%
Secondary Smelter Facilities	Park and Paik (2002)	8-stage Marple cascade impactor sampler 2 Korean facilities (6 samples)	Results blank- and efficiency-corrected	Avg. MMAD (GSD): 4.9 µm (5.0) Avg. lead mass for particles <1 µm: ~25.0%	Avg MMAD (GSD): 15-25 µm (~2.5-8) Avg. lead mass for particles <1 µm: ~1.4-3.3%

Notes: BCI = Battery Council International; GSD = Geometric Standard Deviation; MMAD = Mass Median Aerodynamic Diameter.

Notably, the BCI study results highlight a large amount of variability within and across facility and job categories. Table 3.5 and 3.6 summarize the MMADs reported for various job categories at battery manufacturing facilities and secondary smelter facilities respectively. Across all BMF job categories, the range of MMADs was approximately an order of magnitude. For the SSF facilities, greater variability was observed in the MMADs for the furnace categories compared to other categories. Differences in facility processes or worker activities during sampling events may account for the variability observed across facilities and job categories.

Table 3.5 Summary of Mass Median Aerodynamic Diameters Across Battery Manufacturing Facilities and Job Categories (average of 3 samples collected in each facility/job location) and for All Facilities Combined for Each Job Category (adapted from Petito Boyce *et al*. 2017)

Facility Number	Job Category	N	MMAD Average +/- SD (µm)	MMAD Values[A] (µm)	GSD Values[B]	Average Percent of Lead Mass for Particles <1 µm
1		3	20 +/- 14	5.0; 20; 33	11; 2.9; 3.6	8.6
2		4	25 +/- 4.2	19; 24; 27; 28	2.9; 2.9; 3.0; 2.7	0.16
3		2	10 +/- 7.9	4.6; 16	6.1; 3.2	11
4		3	26 +/- 7.3	19; 25; 34	3.1; 3.2; 3.1	0.27
5	Assembly	3	16 +/- 5.6	9.9; 18; 21	3.3; 3.6; 3.3	1.5
6		2	15 +/- 7.0	9.8; 20	4.0; 4.2	3.4
7		3	15 +/- 7.9	9.0; 12; 24	6.1; 4.1; 3.1	5.1
8		2	34 +/- 7.6	29; 40	3.1; 3.7	0.19
9		2	30+/- 5.8	26; 34	3.3; 7.1	2.0
All Facilities		**24**	**21 +/- 9.5**	**4.6-40 (range)**	**2.7-11 (range)**	**3.3**
1		3	46 +/- 39	21; 26; 90	4.8; 2.6; 6.7	1.2
2		3	47 +/- 16	35; 40; 66	3.7; 5.1; 6.0	0.81
3		3	15 +/- 6.4	7.9; 18; 20	12; 4.6; 17	13
4		3	30 +/- 1.9	28; 31; 32	3.2; 4.2; 3.7	0.48
5	Casting	3	20 +/- 17	8.4; 13; 39	3.3; 3.7; 5.5	2.7
6		3	12 +/- 1.3	11; 11; 13	4.1; 4.3; 4.2	4.4
7		2	60 +/- 6.8	55; 65	6.2; 7.4	1.6
8		3	29 +/- 15	12; 36; 38	2.8; 4.4; 3.6	0.64
9		3	42 +/- 28	22; 30; 73	3.8; 3.7; 4.6	0.60
All Facilities		**26**	**32 +/- 22**	**7.9-90 (range)**	**2.6-17 (range)**	**2.8**
1		3	27 +/- 3.9	22; 28; 30	2.9; 3.3; 3.6	0.28
2		3	35 +/- 4.7	32; 32; 40	3.0; 3.0; 3.4	0.08
3		3	30 +/- 11	18; 30; 41	3.4; 4.1; 4.1	0.68
4		3	21 +/- 4.5	17; 22; 26	2.8; 2.9; 3.1	0.23
5	Pasting	3	15 +/- 7.4	10; 11; 23	2.5; 2.4; 3.2	0.38
6		3	13 +/- 1.5	11; 12; 14	3.9; 5.3; 3.3	3.8
7		3	20 +/- 8.4	12; 19; 29	2.6; 3.9; 3.3	0.71
8		3	34 +/- 17	17; 36; 51	2.6; 3.3; 4.2	0.20
9		3	23 +/- 8.9	13; 25; 31	2.5; 3.9; 3.3	0.43
All Facilities		**27**	**24 +/- 11**	**10-51 (range)**	**2.4-5.3 (range)**	**0.8**

Notes:

GSD = Geometric Standard Deviation; MMAD = Mass Median Aerodynamic Diameter; SD = Standard Deviation.

(A) MMAD values listed in order from smallest to largest. As described in the METHODS/Data Analysis/Statistical Analyses and Data Adjustments section, five outliers were identified in the BMF study data (four in the Assembly job category samples – one each from Facilities 3, 6, 8, and 9; and one in the Casting job category samples – from Facility 7). Outlier data points were not included in the statistical summaries presented in the table above, nor in the subsequent data analyses (*i.e.*, the MPPD modeling or exploratory absorption evaluations).

(B) GSD values listed in order corresponding to MMAD values in MMAD column.

Table 3.6 Summary of Mass Median Aerodynamic Diameters Across Secondary Smelter Facilities and Job Categories (average of 3 samples collected in each facility/job location) and for All Facilities Combined for Each Job Category (adapted from Petito Boyce *et al.*, 2017)

Facility Number	Job Category	N	MMAD Average +/- SD (µm)	MMAD Values[A] (µm)	GSD Values[B]	Average Percent of Lead Mass for Particles <1 µm
1	Blast Furnace	2	13 +/- 16	1.6; 24	41; 2800	40
2		3	16 +/- 7.5	8.5; 15; 23	1.6; 3.3; 2.7	0.42
3		3	18 +/- 2.2	16; 18; 20	2.9; 2.1; 3.9	0.59
4		3	16 +/- 5.0	12; 14; 21	2.1; 2.2; 2.5	0.03
5		3	25 +/- 4.2	21; 25 29	3.5; 4.8; 3.3	0.98
All Facilities		**14**	**18 +/- 7.3**	**1.6-29 (range)**	**1.6-2800 (range)**	**6.1**
1	Casting	3	27 +/- 5.4	21; 29; 31	-11; 5.8; 4.3	4.7
2		3	21 +/- 5.8	15; 20; 27	2.4; 3.1; 2.9	0.19
3		3	14 +/- 2.5	11; 13; 16	2.4; 2.2; 7.1	2.7
4		2	13 +/- 0.97	12; 13	6.3; 5.8	8.0
5		3	33 +/- 4.3	30; 31; 38	3.0; 3.0; 4.0	0.20
All Facilities		**14**	**22 +/- 8.8**	**11-38 (range)**	**2.2-11 (range)**	**2.8**
1	Material Handling	3	17 +/- 2.0	15; 16; 19	3.0; 2.8; 2.8	0.45
2		3	16 +/- 3.8	13; 14; 20	2.3; 2.0;- 2.3	0.05
3		2	14 +/- 2.3	12; 15	2.7; 2.7	0.48
4		3	15 +/- 1.7	13; 15; 16	2.0; 2.7; 4.2	0.97
5		2	16 +/- 0.7	16; 17	2.6; 2.6	0.17
All Facilities		**13**	**15 +/- 2.3**	**12-20 (range)**	**2.0-4.2 (range)**	**0.44**
1	Refining	3	25 +/- 7.2	17; 25; 31	3.0; 6.3; 5.0	2.0
2		3	29 +/- 14	17; 27; 44	2.2; 3.1; 2.6	0.07
3		3	23 +/- 6.5	18; 20; 30	4.4; 2.9; 3.7	1.1
4		3	19 +/- 10	12; 14; 30	2.4; 3.2; 3.7	0.64
5		3	22 +/- 5.8	17; 21; 28	3.6; 3.1; 4.8	1.2
All Facilities		**15**	**23 +/- 8.5**	**12-44 (range)**	**2.2-6.3 (range)**	**1.0**
1	Reverb Furnace	3	14 +/- 11	3.5; 15; 24	8.3; 6.1; 2.4	12
2		3	18 +/- 6.1	13; 15; 25	3.1; 2.8; 4.4	0.48
3		3	19 +/- 12	11; 14; 33	2.8; 3.0; 4.4	0.88
5		3	51 +/- 39	20; 39; 95	3.0; 3.3; 5.4	0.26
All Facilities		**12**	**25 +/- 24**	**3.5-95 (range)**	**2.4-8.3 (range)**	**3.3**

Notes:

GSD = Geometric Standard Deviation; MMAD = Mass Median Aerodynamic Diameter; SD = Standard Deviation.

(A) MMAD values listed in order from smallest to largest. As described in the METHODS/Data Analysis/Statistical Analyses and Data Adjustments section, two outliers were identified in the SSF study data (one in the Blast Furnace job category samples from Facility 1 and one in the Casting job category samples from Facility 4). Outlier data points were not included in the statistical summaries presented in the table above, nor in the subsequent data analyses (*i.e.*, the MPPD modeling or exploratory absorption evaluations).

(B) GSD values listed in order corresponding to MMAD values in MMAD column.

Such variability within and across facility and job categories may account for some of the differences observed between previously published data and the BCI study results. Alternatively, differences may be attributable to the broader range of job categories included in the BCI study, or possible differences between processes and controls in Korean and US industries. For example, hygiene or other exposure control mechanisms employed in newer facilities may reduce exposure routes including ingestion of particles that may accumulate on worker hands during smoke breaks or lunch breaks. Furthermore, exposure control mechanisms may impact particle size distributions, with subsequent impacts on particle deposition in the lung and impacts on blood lead. Issues related to variability within and across facility and job categories, as well the implications of exposure controls in newer facilities, suggest that the more limited Park and Paik (2002) data may not be representative of industry wide exposure conditions and particle size distributions, particularly for US secondary smelters.

These findings from the BCI studies and other studies in the scientific literature indicate that the PSD data used by OEHHA in its MPPD modeling is not fully representative of likely exposure conditions in US industries and forms an insufficient basis for modeling to support evaluations of occupational exposure limits. In particular, such modeling should not be limited to the 1-15 µm MMAD size range, because available data indicate that workplace settings exist with average MMAD values that are greater than this range. By incorporating data such as the findings from the BCI studies in its modeling efforts, OEHHA would expand the particle size range, geographic coverage, sampling time frame, and sample size reflected in its analyses.

3.4 Other Recommendations

Several other components of the OEHHA analyses merit additional documentation and discussion. In particular, OEHHA should better document and justify certain key choices made in the modeling process, including demonstrating that its choices reflect a systematic and critical review of the scientific literature and other relevant information. As noted above, these components include the Agency's justification for relying primarily on the PSD data collected by Park and Paik (2002) as inputs for its MPPD modeling and additional evaluation of the limitations in the scientific foundation for the GI absorption estimates used in its modeling. The OEHHA report should also include a more rigorous evaluation of its GSD selection process and the degree to which the selected value is likely to represent inherent interindividual- or worker population-level variability. In particular, the report should acknowledge that the comparison GSDs that OEHHA calculated based on worker data reflect older studies (the most recent study reviewed was published in 1981) and thus may not be representative of current worker exposure patterns.

In a related issue, the OEHHA report should further discuss the implications of using data from older workplace studies to conduct initial modifications to the PBPK model and validate the final model predictions. Again, a primary topic that should be discussed is the issue of whether the model developed based on data reflecting studies of older workplace conditions provides a suitable basis for estimating potential exposures in current worker populations. For example, one of the two studies that OEHHA relied on to assess the performance of the Leggett+ model was a study of battery factory workers (Williams *et al*., 1969). In other evaluations of this study, it has been specifically noted as an exposure setting where "hand to mouth lead transfer" and "personal working habits" may have played an important role in the observed PbB levels (Hammond *et al*., 1981). Similarly, the OEHHA report should also further consider the degree to which the model predictions are consistent with and representative of observations in current workplaces.

In considering the validity of the Leggett model predictions, OEHHA should also consider concerns regarding the technical validity and accuracy of the Leggett model that have arisen in previous model applications. In its modeling efforts, OEHHA noted that its initial case study applications of the Leggett model resulted in "significant under predictions" of worker PbB levels, and that they needed to adjust the model to yield predicted PbB concentrations that more closely matched observed levels. In previous applications of the Leggett model to assess community lead exposures in children (*e.g.*, in components of US EPA's evaluation of the National Ambient Air Quality Standard for lead [as documented in US EPA, 2013]), the Leggett model has yielded higher predicted PbB levels than other models (*e.g.*, US EPA's Integrated Exposure Uptake Biokinetic [IEUBK] model or the O'Flaherty model; US EPA, 2006). In another application, US EPA's Science Advisory Board (SAB) supported the Agency's decision to conduct evaluations of adult lead exposures using its Adult Lead Model[4] (ALM) rather than the Leggett model when developing lead dust standards for residences. Specifically, the SAB stated that in that application the ALM "yields more plausible estimates of average population PbB concentrations" than the Leggett model (US EPA SAB, 2011). Similarly, for the corresponding evaluations of children's lead exposures, the SAB identified US EPA's IEUBK model as "the clearly preferred model" rather than the Leggett model. These concerns indicate the need for careful validation and interpretation of the Leggett/Leggett+ model results before relying on the Leggett+ model to support regulatory decisions.

[4] US EPA's ALM is a simplified steady-state model that uses a set biokinetic slope factor to estimate a PbB concentration corresponding to an estimated daily intake of lead.

4 Implications of Recommended Corrections and Modifications for Modeling Results

This section summarizes the differences between the OEHHA modeling approach and the recommended corrected/modified approach. Example calculations are provided, illustrating the quantitative implications of the recommended changes for the modeling results. In particular, these analyses focus on the implications of the changes for the calculated ITC values and the PbB concentrations predicted to be associated with specific PbA concentrations. It is noted, however, that this discussion does not imply endorsement of the use of the OEHHA modeling approach to support regulatory decision-making, even if the recommended corrections and modifications are undertaken. As discussed in this review, even if the proposed changes are made, other fundamental concerns regarding the OEHHA approach will remain and require further evaluation (*e.g.*, questions regarding the validity of the Leggett+ model predictions for current workplace conditions , particularly in light of OEHHA's use of older studies that are unlikely to be reflective of current conditions in its model validation efforts).

The recommended corrections and modifications to the OEHHA modeling approach described above result in the following changes to the model predictions:

- For all particle sizes, a fraction of deposited particles are completely cleared from the body (*e.g.*, through nose blowing), and thus are never cleared to the GI tract or absorbed;
- For all particle sizes, a smaller fraction of particles are cleared to the GI tract during fasting conditions (*i.e.*, under the highest assumed GI absorption conditions); and
- For larger particles, a smaller fraction of particles are deposited in the respiratory tract.

All of these modifications result in a smaller fraction of the lead from inhaled airborne particles being absorbed into the body. As a result, using the corrected/modified approach, the PbB concentration predicted to be associated with a specific PbA concentration is reduced and the PbA concentration associated with a specific target PbB concentration is increased.

In addition, calculations using the modified approach demonstrate that a central conclusion of the OEHHA report is not correct. In contrast to statements made in the OEHHA report, the ITC calculation does in fact differ depending on the particle size distribution to which exposure occurs (including consideration of particles in the 1-15 μm and greater MMAD size range), particularly when considering the appropriate adjustment for larger sized particles in the MPPD model. As a result, this important feature of workplace exposure characterization must be appropriately addressed in determining health-protective, scientifically sound workplace exposure levels, *i.e.*, by applying the corrections and modifications described in this review.

4.1 Implications for ITC Values

A number of calculations were undertaken to explore the implications of these recommended modifications for the OEHHA modeling results. As a first step, the impacts of the modifications on the calculated ITC values were explored. These calculations were conducted using various combinations of the following model assumptions:

- Applying the modified clearance approach to estimate the lead absorption (as reflected in the ITC) associated with various particle deposition distributions generated by the MPPD model;
- Correcting the MPPD model analyses for larger particle sizes (MMAD > 8 µm) by applying the IAF; and
- Applying an assumed particle size (MMAD = 20 µm or greater) in the MPPD model that is greater than that evaluated in the OEHHA report (MMAD up to 15 µm) to estimate the impact of larger particle sizes on deposition in the three regions of the respiratory tract.

Various particle sizes and activity levels were considered in these calculations.

As illustrated by the evaluations summarized in Table 4.1, these corrections and modifications confirm that the ITC value is in fact highly influenced by particle size and related assumptions (including consideration of particles in the 1-15 µm and greater MMAD size range). In addition, consideration of updated knowledge regarding particle clearance also substantially affects the ITC calculation. Specifically, the first row of this table lists the ITC value (0.3, or 30%) that OEHHA reported from its calculations for a variety of particle sizes (up to an MMAD of approximately 15 µm) and exposure conditions. As noted above, its calculations did not include use of the IAF for particle sizes > 8 µm. The next section of Table 4.1 (OEHHA Baseline) illustrates the changes in the ITC that result when the IAF is applied for an assumed particle size of 14 µm in the MPPD model (the particle size used in the OEHHA modeling based on BMF data) and/or when the modified clearance approach is included in the ITC calculations. As can be seen, when both of these corrections/modifications are made, the resulting ITC (0.16-0.17) is approximately one-half of the value originally derived by OEHHA.

Table 4.1 Impacts of Modifications on Inhalation Transfer Coefficient Values

Analysis	Modifications	Resulting ITC[a]
OEHHA Baseline (larger or smaller particles)	–	0.3
OEHHA Baseline (larger particles)[b]	Add IAF only	0.25-0.28
	Add modified clearance approach only	≈0.2
	Add modified clearance approach and IAF	0.16-0.17
BCI BMF Baseline[c]	Includes larger particle size and IAF	0.16
	Add modified clearance approach	≈0.1
OEHHA (smaller particles)[d]	Add modified clearance approach	0.22-0.23

Notes:
BCI = Battery Council International; BMF = battery manufacturing facility; IAF = Inhalability Adjustment Factor; ITC = Inhalation Transfer Coefficient; OEHHA = Office of Environmental Health Hazard Assessment.
(a) Range in ITC values reflects differences observed for different assumed activity levels.
(b) Calculations conducted using MMAD = 14.1 µm, the value for BMFs used in the OEHHA analyses.
(c) Calculations conducted using MMAD = 20 µm, reflecting the high end of the particle size distribution range identified in the MPPD model documentation, as well as observations reflected in the results from the BCI BMF and SSF Studies.
(d) Calculations conducted using MMAD = 4.9 µm, the value for SSFs used in the OEHHA analyses.

Similarly, as shown in the next section of Table 4.1 (BCI BMF Baseline), when a larger particle size is employed (*e.g.*, a particle size of 20 µm to reflect the high end of the particle size distribution range identified in the MPPD model documentation, as well as observations reflected in the results from the BCI BMF and SSF Studies), substantial reductions in the ITC are observed. When the larger particle size is used and the IAF is correctly applied, the calculated ITC of 0.16 is again determined to be approximately one-half of the value originally derived by OEHHA. When the modified clearance approach is also included, the calculated ITC drops to approximately one-third of the value originally derived by OEHHA (*i.e.*, ≈0.1). As discussed below, consideration of additional modifications to these calculations indicates that ITC values less than 0.1 could be derived for some sets of exposure assumptions.

Figure 4.1 graphically illustrates some of the impacts of the recommended changes on the modeling results. This figure compares results from the MPPD model for the OEHHA Baseline modeling for larger particles (*i.e.*, excluding the IAF and reflecting a particle size of 14 µm and a GSD of 1.5) and MPPD results obtained using a larger particle size (*i.e.*, 20 µm and a GSD of 4) and the IAF. As can be seen, applying just these changes in the MPPD modeling yields dramatically different results. In particular, the percentage of particles predicted to be deposited in the ET region decreases by approximately one-third to more than one-half of the amount predicted by the original OEHHA analyses (*i.e.*, a decrease in the deposition fraction from 0.89 to 0.58 for the calculations reflecting moderate activity and a decrease from 0.97 to 0.44 for the calculations reflecting resting conditions).

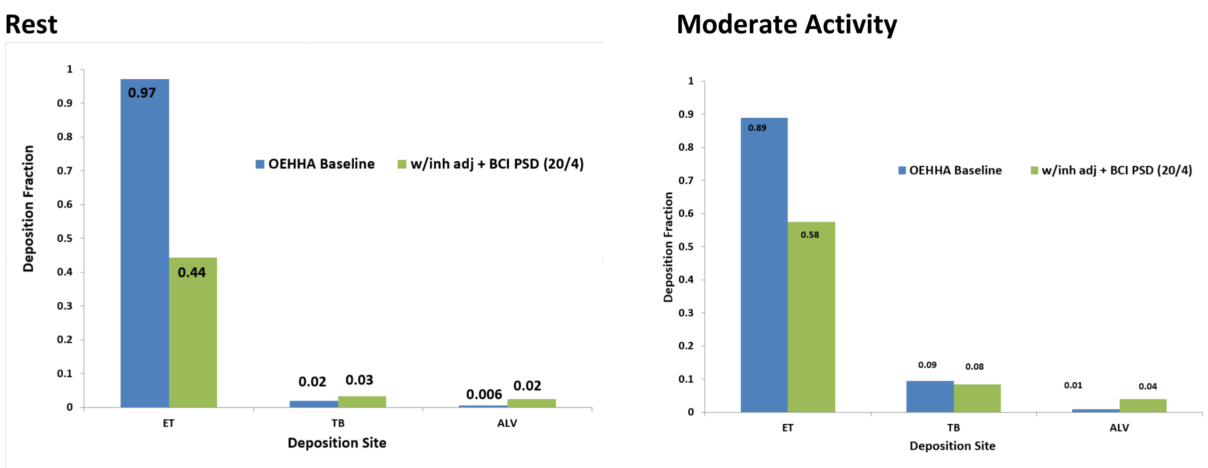


Figure 4.1 Implications of Including the Inhalability Adjustment Factor and Larger Particle Size for Multiple-Path Particle Dosimetry Modeling Results

The last section of Table 4.1 (OEHHA [small particles]) demonstrates that, even for small particles, OEHHA's original ITC of 0.3 does not reflect likely lead absorption from these particles. Specifically, when OEHHA baseline analyses for smaller particles (*e.g.*, ~5 µm, the size range that OEHHA assessed for SSFs) are adjusted to reflect the modified clearance approach based on updates to the ICRP model, the resulting ITC is reduced from 0.3 to 0.22-0.23 (22-23%).

As noted in the supporting documentation described in this review, a number of the corrections and modifications reflected in Table 4.1 represent conservative (*i.e.*, health-protective) assumptions, that is, they may overestimate particle deposition and lead absorption. For example, studies in the scientific literature and the calculations provided by Dr. Leggett during his review of the OEHHA report indicate that the percentage of deposited particles subject to rapid clearance processes could be greater than assumed in the calculations underlying Table 4.1. Similarly, exploratory calculations using the MPPD model indicate decreases in model predictions of particle deposition with increases in particle size to values > 20 µm.[5] Clearance from the body by processes such as nose blowing, and the duration of food intake impacts on GI absorption of lead, could also be greater than assumed in the Table 4.1 calculations.

Exploratory calculations indicate that some combinations of alternative modifications to these assumptions could yield an ITC that is even less than the values reported in Table 4.1. For example, the combination of the following modified assumptions yields an ITC value of 0.07 (7%):

- Using the largest particle size observed in the BCI studies (32 µm), with a GSD of 5 and assuming resting conditions;
- Assuming a greater percentage of deposited particles undergo rapid clearance processes (*i.e.*, 70% for the ET region and 100% for the TB region), and thus are not subject to GI absorption under fasting conditions;
- Assuming that 20% of deposited particles are removed *via* nose blowing; and
- Assuming that the duration of "fed" conditions in the GI tract is 6 hours per day (rather than 4 hours) and that the duration of "between-meal" conditions is correspondingly reduced.

These analyses demonstrate that OEHHA's conclusion that particle size (including consideration of particles in the 1-15 µm MMAD size range) does not affect overall lead absorption (as reflected in the ITC) is incorrect and not supported by current scientific knowledge regarding particle deposition and clearance. As illustrated in Table 4.1, particle size clearly influences the ITC calculation using the corrected and updated model. Moreover, for workplaces with predominantly larger particle sizes (such as those included in the BCI studies), a more appropriate value for the ITC is closer to 0.1, or possibly lower, rather than the 0.3 value calculated in the OEHHA report. In addition, even for smaller particle sizes, including the updated science regarding particle clearance yields ITC estimates that are less than the value calculated by OEHHA (*e.g.*, 0.22 or 0.23 *vs*. 0.3).

As a result, these analyses call into question both the OEHHA modeling results and their soundness as a basis for determining occupational exposure levels. Moreover, the modified estimates represent conservative changes to the ITC calculation. Alternative assumptions can yield ITC estimates that are even lower, which would result in lower predicted PbB concentrations for specific PbA concentrations. Because the ITC value has such important implications for the PbB concentrations predicted to be associated with specific PbA exposures, these types of analyses warrant careful consideration in conducting the modeling to support determination of occupational exposure limits. Without these corrections and modifications, the current OEHHA analyses are incorrect and inadequate for supporting policy decision-making.

4.2 Implications for PbB Predictions

Additional analyses were undertaken to explore the implications of the recommended changes for the PbB levels predicted to be associated with specific PbA concentrations using the OEHHA modeling approach. The modeling results derived by OEHHA (CalEPA, 2013) are summarized in Table 4.2. Table 4.3 provides example results obtained using benchmark alternative values for the ITC, reflecting the range of

[5] Although the MPPD model documentation indicates that the target size range for model analyses is from < 0.01 to ~20 µm, the model accommodates input values that are greater than 20 µm (Price, 2014). Using MMAD values ranging from 20 to 32 µm (the maximum average MMAD value observed in the BCI studies), a GSD of 4, and assuming resting conditions, the predicted total deposition fraction decreased from 0.51 to 0.45. The observations for the three regions of the respiratory tract are as follows: from 0.48 to 0.42 for the ET region, from 0.009 to 0.02 for the TB region, and no change for the ALV region.

values derived based on the recommended model changes (as summarized in Table 4.1; *i.e.*, correctly using the IAF for larger particle sizes, updating the clearance and absorption assumptions, and expanding the particle size range considered) and including consideration of the potential for even lower ITC values to be obtained using alternative assumptions (*i.e.*, using an example benchmark ITC value of 0.05 to explore the implications of such calculations). As can be seen in Table 4.3, when the ITC is decreased by a factor of 3, the PbA concentration estimated to be associated with a specific 95th percentile PbB concentration increases by a factor of approximately 3; for example, for a target 95th percentile PbB concentration of 20 μg/dL, the corresponding PbA concentration increases from 5.9 μg/m^3 (using the OEHHA baseline assumptions, including an ITC value of 0.3) to 17.6 μg/m^3 (using the recommended changes, including an ITC value of 0.1). If the ITC is decreased by a greater amount (*e.g.*, the factor of 6 decrease that would be represented by an ITC value of 0.05), the PbA concentration would be increased by a corresponding greater amount.

Table 4.2 Overview of OEHHA Modeling Results

8-hr TWA PbA (μg/m^3)	Predicted PbB (μg/dL) 95th percentile
0.5	5
2.1	10
6.0	20
10.4	30

Notes:
TWA = time-weighted average; PbA = air lead; PbB = blood lead; OEHHA = Office of Environmental Health Hazard Assessment.
Excerpt from Table S-1 of CalEPA (2013).

Table 4.3 Summary of Impacts of Alternative Inhalation Transfer Coefficient Values on Air Lead Results

95th Percentile PbB (μg/dL)	50th Percentile PbB (μg/dL)	PbA (μg/m^3)			
		@ ITC = 0.3	@ ITC = 0.2	@ ITC = 0.1	@ ITC = 0.05
5	2.3	0.5	0.7	1.5	2.9
10	4.6	2.1	3.2	6.4	12.8
20	9.3	5.9	8.8	17.6	35.2
30	13.9	10.3	15.5	30.9	61.9

Notes:
ITC = Inhalation Transfer Coefficient; PbA = air lead; PbB = blood lead.

As discussed above, by implementing the recommended changes, the modeling will eliminate the specific errors in the modeling approach described above and yield results that better reflect the current state of the science. These changes are needed to provide a meaningful basis for determining health-protective occupational exposure limits, particularly for certain types of workplaces. In particular, the current OEHHA model results overestimate the mass of inhaled particles that will be deposited in the respiratory tract and the fraction of inhaled lead that will be deposited and absorbed into the body. The current approach also led OEHHA to incorrectly conclude that particle size (including consideration of particles in the 1-15 μm MMAD size range) does not affect the fraction of lead from airborne particulates that will be transferred to the blood (*i.e.*, following inhalation, deposition, and absorption). Consequently, the model yields inaccurate predictions of the PbB concentrations that would be associated with specific PbA concentrations, and does not provide a sound basis for evaluating potential workplace exposures or standards. As a result, OEHHA should conduct additional modeling applying the recommended changes to provide a scientifically sound foundation for setting occupational exposure limits.

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