

EXECUTIVE SUMMARY

E.1 INTRODUCTION

This document critically assesses the latest scientific information concerning health and welfare effects associated with the presence of various concentrations of lead (Pb) in ambient air, as pertinent to providing updated scientific bases for EPA's periodic review of the National Ambient Air Quality Standards for Lead (Pb NAAQS). As such, this document builds upon previous assessments published by the U.S. Environmental Protection Agency (EPA), including: (a) the 1977 EPA document, *Air Quality Criteria for Lead*; (b) an updated revision of that Lead Air Quality Criteria Document and an accompanying Addendum published in 1986 (1986 Pb AQCD/Addendum); and (c) the associated 1990 Supplement to the 1986 Pb AQCD/Addendum. This document focuses on evaluation and integration of information relevant to Pb NAAQS criteria development that has become available mainly since that covered by the 1986 and 1990 criteria assessments.

E.1.1 Clean Air Act Legal Requirements

As discussed in Chapter 1 of this revised Pb AQCD, Sections 108 and 109 of the Clean Air Act (CAA) govern establishment, review, and revision of U.S. National Ambient Air Quality Standards (NAAQS):

- Section 108 directs the U.S. Environmental Protection Agency (EPA) Administrator to list ubiquitous (widespread) air pollutants that may reasonably be anticipated to endanger public health or welfare and to issue air quality criteria for them. The air quality criteria are to reflect the latest scientific information useful in indicating the kind and extent of all exposure-related effects on public health and welfare expected from the presence of the pollutant in the ambient air.
- Section 109 directs the EPA Administrator to set and periodically revise, as appropriate, two types of NAAQS: (a) primary NAAQS to protect against adverse health effects of listed criteria pollutants among sensitive population groups, with an adequate margin of safety, and (b) secondary NAAQS to protect against welfare effects (e.g., impacts on vegetation, crops, ecosystems, visibility, climate, man-made materials, etc.). Section 109 also requires peer review of the NAAQS and their underlying scientific bases by the Clean Air Scientific Advisory Committee (CASAC), a committee of independent non-EPA experts.

1 E.1.2 Chronology of Lead NAAQS Revisions

- 2 • In 1971, U.S. EPA promulgated national ambient air standards for several major “criteria”
3 pollutants (see Federal Register, 1971) that did not include lead at that time. Later, on
4 October 5, 1978, the EPA did promulgate primary and secondary NAAQS for lead, as
5 announced in the Federal Register (1979). The primary standard and the secondary standard
6 are the same: 1.5 $\mu\text{g}/\text{m}^3$ as a calendar quarterly average (maximum arithmetic mean
7 averaged over 90 days). The standards were based on the EPA’s 1977 document, *Air Quality*
8 *Criteria for Lead*.
- 9 • In 1986, the EPA published a revised Pb AQCD that assessed newly available scientific
10 information published through December 1985. That 1986 document was mainly concerned
11 with Pb health and welfare effects, but other scientific data were also discussed to provide a
12 better understanding of the pollutant in the environment. Thus, the Pb AQCD included
13 chapters that discussed the atmospheric chemistry and physics of the pollutant; analytical
14 approaches; environmental concentrations; human exposure and dosimetry; physiological,
15 toxicological, clinical, epidemiological aspects of lead health effects; and lead effects on
16 ecosystems. An Addendum to the 1986 Lead AQCD was also published concurrently.
- 17 • Subsequently, a supplement to the 1986 Lead AQCD/Addendum was published in 1990.
18 That 1990 Supplement evaluated still newer information emerging in the published literature
19 concerning (a) lead effects on blood pressure and other cardiovascular endpoints and (b) the
20 effect of lead exposure during pregnancy and/or during the early postnatal period on birth
21 outcomes and/or on the neonatal physical and neuropsychological development of infants
22 and children.
- 23 • Evaluations contained in the 1986 Lead AQCD/Addendum and 1990 Supplement provided
24 scientific inputs to support decision making regarding periodic review and, as appropriate,
25 revision of the Pb NAAQS, and they were drawn upon by EPA’s Office of Air Quality
26 Planning and Standards (OAQPS) in preparation of a 1990 OAQPS Lead Staff Paper. After
27 consideration of evaluations contained in these documents, EPA chose not to propose
28 revision of the Pb NAAQS. At that time, as part of a broad 1991 U.S. EPA Strategy for
29 Reducing Lead Exposure, the Agency focused on regulatory and remedial clean up efforts to
30 reduce Pb exposure from non-air sources and media judged to pose more significant public
31 health risks to U.S. populations than remaining air emissions. By 1990, annual average
32 ambient air Pb levels had dropped in U.S. urban areas to about 0.15-0.25 $\mu\text{g}/\text{m}^3$ due to
33 phasedown of leaded gasoline.
- 34 • This revised Pb AQCD, prepared by EPA’s National Center for Environmental Assessment
35 (NCEA), provides scientific bases to support Clean Air Act-mandated periodic review of the
36 Pb NAAQS. The document assesses the latest available scientific information (published
37 mainly through December 2005) judged to be useful in deriving criteria as scientific bases for
38 decisions on possible revision of the current Pb NAAQS.
- 39 • A separate EPA Lead Staff Paper, prepared by OAQPS in EPA’s Office of Air and Radiation
40 (OAR), will draw upon key findings/conclusions from this document and, together with other
41 analyses, will develop and present options for consideration by the EPA Administrator
42 regarding review, and possible revision, of the Pb NAAQS.

1 **E.1.3 Document Organization and Structure**

2 Volume I of this document consists of the present Executive Summary and eight main
3 chapters of this revised Pb AQCD. Those main chapters focus primarily on interpretative
4 evaluation of key information, whereas more detailed descriptive summarization of pertinent
5 studies and/or supporting analyses are provided in accompanying annexes. Volume II contains
6 (a) the annexes for Chapters 5 and 6 (which assess toxicologic and epidemiologic evidence
7 regarding Pb health effects) and (b) the annex for Chapter 7 (which assesses information on Pb
8 ecological effects).

9 Topics covered in the main chapters of the present AQCD are as follows:

- 10 • This Executive Summary summarizes key findings and conclusions from Chapters 1 through
11 8 of this revised Pb AQCD, as they pertain to background information on Pb-related
12 atmospheric science and air quality, human exposure aspects, dosimetric considerations,
13 health effect issues, and environmental effect issues.
- 14 • Chapter 1 provides a general introduction, including an overview of legal requirements,
15 the chronology of past revisions of Pb-related NAAQS, and orientation to the structure of
16 this document.
- 17 • Chapters 2 and 3 provide background information on chemistry/physics of Pb, atmospheric
18 transport and fate, air quality, and multimedia exposure aspects to help to place the ensuing
19 discussions of Pb health and welfare effects into perspective.
- 20 • Chapters 4 through 6 assess dosimetry aspects, toxicologic (laboratory animal) studies, and
21 epidemiologic (observational) studies of Pb health effects.
- 22 • Chapter 7 assesses information concerning environmental effects of Pb on terrestrial and
23 aquatic ecosystems, to support secondary Pb NAAQS decision making.
- 24 • Chapter 8 then provides an integrative synthesis of key findings and conclusions derived
25 from the preceding chapters with regard to ambient Pb concentrations, human exposures,
26 dosimetry, health effects of importance for primary Pb NAAQS decisions, and ecosystem
27 effects pertinent to secondary Pb NAAQS decisions.

28 29 30 **E.2 AMBIENT LEAD SOURCES, EMISSIONS, AND TRANSPORT**

- 31 • Overall, current ambient Pb concentrations in the U.S. are generally well below the NAAQS
32 level, except for locations influenced by local sources. During 2000 to 2004, on average,
33 quarterly mean Pb concentrations at Federal Reference Method monitors ranged from 0.10 to
34 0.22 $\mu\text{g}/\text{m}^3$ (including point source-related monitors). In the same time period, only one to

1 five locations from among ~200 U.S. sites measured quarterly maximum Pb levels that
2 exceeded the NAAQS level ($1.5 \mu\text{g}/\text{m}^3$, quarterly max average) in any given year.

- 3 • Historically, mobile sources were a major source of lead emissions, due to the use of leaded
4 gasoline. The United States initiated the phasedown of gasoline Pb additives in the late
5 1970s and intensified the phase-out of Pb additives in 1990. Accordingly, airborne Pb
6 concentrations have fallen dramatically nationwide, decreasing an average of 94% between
7 1983 and 2002. This is considered one of the great public and environmental health
8 successes. Remaining mobile source-related emissions of Pb include brake wear,
9 resuspended road dust, and emissions from vehicles that continue to use leaded gasoline
10 (e.g., some types of aircraft and race cars).
- 11 • Currently, the major stationary sources of Pb are in the industrial sector, including iron and
12 steel foundries and combustion sources, e.g., energy generation through coal and fuel oil
13 combustion, or wood combustion and hazardous or solid waste incineration. Other sources
14 include Pb-acid battery plants, primary and secondary Pb smelters, lead-alloy production
15 facilities, smelters for other metals, such as copper or nickel; cement manufacturing; and Pb
16 mining and/or processing.
- 17 • The resuspension of soil-bound lead particles and contaminated road dust is a significant
18 source of airborne lead. In general, the main source of resuspension is wind and vehicular
19 traffic, although resuspension through other mechanical processes such as construction,
20 pedestrian traffic, agricultural operations, and even raindrop impaction is possible. Elevated
21 lead levels are found in soil near stationary lead sources and roadways that were heavily
22 trafficked prior to gasoline-Pb phasedown; and soil lead can also be elevated near hazardous
23 waste cleanup sites.
- 24 • Lead can be transported in the atmosphere through mechanisms including deposition and
25 resuspension of Pb-containing particles. Dry deposition is the process by which pollutants
26 are removed from the atmosphere in the absence of precipitation. The size of depositing
27 particles is arguably the most important factor affecting dry deposition rates. Wet deposition
28 is the process by which airborne pollutants are scavenged by precipitation and removed from
29 the atmosphere. The size of particles can also influence wet deposition rates, with large
30 particles being scavenged more efficiently and, hence, tending to be removed closer to their
31 source of emission than small particles.

34 **E.3 MULTIMEDIA EXPOSURE PATHWAYS**

- 35 • Exposure to Pb occurs through a number of routes. In addition to exposure to Pb in the air,
36 other major environmental routes for exposure to lead include: Pb in drinking water; Pb-
37 contaminated food; Pb in house dust; and Pb-based paint in older homes. Also, other Pb
38 exposure sources vary in their prevalence and potential risk, such as calcium supplements,
39 Pb-based glazes, and certain kinds of miniblinds, hair dye, and other consumer products.

- 1 • Lead in drinking water results primarily from corrosion of Pb pipes, Pb-based solder, or brass
2 or bronze fixtures within a residence; very little Pb in drinking water comes from utility
3 supplies. Lead in drinking water, although typically found at low concentrations in the
4 United States, has been linked to elevated blood Pb concentrations in some U.S. locations.
- 5 • Although marked reductions of Pb in U.S. market basket food supplies have occurred during
6 the past several decades, Pb-contaminated food still can be a major route of Pb exposure for
7 some individuals. It was estimated that in 1990, North Americans ingested ~50 µg of lead
8 each day through food, beverages, and dust; with ~30 to 50% of this amount via food and
9 beverages. With the elimination of Pb solder in U.S. canned food, food-Pb intake has fallen
10 dramatically in the United States. Data from U.S.D.A. 1994-1996 total diet studies showed
11 96% decreases for 2-5 year olds (from 30 to 1.3 µg Pb per day) and 93% in adults (from 35
12 to 2.5 µg Pb per day) compared to 1982-1984 levels. Some imported canned goods,
13 especially from countries where Pb-soldered cans are still not banned, can be a source of
14 notable dietary-Pb intake for some U.S. population groups, as can Pb-glazed storage pottery.
- 15 • Lead-based paint exposure has long been one of the most common causes of clinical Pb
16 toxicity. Lead-based paint was the dominant form of house paint for many decades, and a
17 significant percentage of homes still contain lead-based paint on some surfaces. Lead from
18 deteriorating paint can be incorporated into exterior residential soils and/or house dust. The
19 associated Pb exposure is often due to ingestion from hand-to-mouth activities and pica,
20 which are common in children. Inhalation Pb exposure of adults and children can also be
21 increased markedly during renovation or demolition projects.
- 22 • Given the large amount of time people spend indoors, exposure to Pb in dusts and indoor air
23 can be significant. For children, dust ingested via hand-to-mouth activity is often a more
24 important source of Pb exposure than inhalation. Dust can be resuspended through
25 household activities, thereby posing an inhalation risk as well. House dust Pb can derive
26 both from Pb-based paint and from other sources outside the home. The latter include
27 Pb-contaminated airborne particles from currently operating industrial facilities or
28 resuspended soil particles contaminated by deposition of airborne Pb from past emissions.
- 29 • In the US, decreases in mobile sources of lead, resulting from the phasedown of gasoline Pb
30 additives, created a 98% decline in emissions from 1970 to 2003. NHANES data show a
31 consequent parallel decline in blood-Pb levels in children aged 1 to 5 years from a geometric
32 mean of ~15 µg/dL in 1976-1980 to ~1-2 µg/dL in the 2000-2004 period.

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35 **E.4. TOXICOKINETICS AND MEASUREMENT/MODELING OF**
36 **HUMAN EXPOSURE IMPACTS ON TISSUE DISTRIBUTION**
37 **OF LEAD**

38 At the time of the 1986 Lead AQCD, it was noted that external Pb exposures via various
39 routes (inhalation, ingestion, dermal) were reflected by increased blood-Pb concentrations, which

1 served as a key biomarker of Pb exposure and index by which to judge risk of Pb-induced health
2 effects. It was also recognized (a) that lead distributed to and accumulated in several bone
3 compartments and (b) that bone lead might as a source of long-term internal exposure. Important
4 findings from newly available studies include the following:

- 5 • Blood Pb is found primarily (~99%) in red blood cells. It has been suggested that the small
6 fraction of Pb in plasma (<0.3%) may be the more biologically labile and toxicologically
7 active fraction of the circulating lead. The relationship between lead intake and blood lead
8 concentration is curvilinear; i.e., the increment in blood lead concentration per unit of lead
9 intake decreases with increasing blood lead concentration.
- 10 • New studies investigating the kinetics of lead in bone have demonstrated that bone lead
11 serves as a blood lead source years after exposure and as a source of fetal lead exposure
12 during pregnancy.
- 13 • Whereas bone lead accounts for ~70% of the body burden in children, in human adults, more
14 than 90% of the total body burden of lead is found in the bones. Lead accumulation is
15 thought to occur predominantly in trabecular bone during childhood and in both cortical and
16 trabecular bone in adulthood.
- 17 • A key issue of much importance in carrying out risk assessments that estimate the potential
18 likelihood of Pb-induced health effects is the estimation of external Pb-exposure impacts on
19 internal Pb tissue concentrations. This includes the estimation of typical Pb-exposure
20 impacts on internal distribution of lead to blood and bone (as key biomarkers of Pb
21 exposure), as well as to other “soft tissue” target organs (e.g., brain, kidney, etc.).
- 22 • Earlier criteria assessments in the 1977 and 1986 Pb AQCDs extensively discussed the
23 available slope factor and/or other regression models of external Pb exposure impacts on
24 blood Pb concentration in human adults and children. Further refinements in regression
25 modeling of lead impacts on blood or bone lead are discussed in Chapter 4 of this document.
- 26 • The older slope factor analyses discussed in the 1977 and 1986 Pb AQCDs noted that at
27 relatively low air-Pb concentrations ($\leq 2 \mu\text{g}/\text{m}^3$), pediatric blood-Pb levels generally increase
28 by $\sim 2 \mu\text{g}/\text{dL}$ per each $1 \mu\text{g}/\text{m}^3$ increment in air-Pb concentration.
- 29 • Several new empirical analyses have shown that a child’s blood lead is strongly associated
30 with interior dust lead loading and its influence on hand lead. Both exterior soil and paint
31 lead contribute to interior dust lead levels. Not all ingested lead is absorbed to the same
32 extent. Factors such as an individual’s age and diet, as well as chemical and physical
33 properties of Pb compounds and the media they occur in, affect absorption, e.g. absorption is
34 increased by fasting and dietary deficiencies in either iron or calcium. It has been estimated
35 that for every 1000 ppm increase in soil-Pb concentration, pediatric blood-Pb levels generally
36 increase by ~ 1 to $5 \mu\text{g}/\text{dL}$ in infants and children < 6 years old. However, intake of soil-Pb
37 with low bioaccessibility or bioavailability characteristics can yield distinctly lower-than-
38 typical blood-Pb increments.

- 1 • Information on lead biokinetics, bone mineral metabolism, and lead exposures has led to
2 refinements and expansions of pharmacokinetic models. Three pharmacokinetic models are
3 currently being used or are being considered for broad application in lead risk assessment:
4 (1) the Integrated Exposure Uptake BioKinetic (IEUBK) model for lead in children
5 developed by EPA (U.S. Environmental Protection Agency, 1994a,b; White et al., 1998);
6 (2) the Leggett model, which simulates lead kinetics from birth through adulthood (Leggett,
7 1993); and (3) the O’Flaherty model, which simulates lead kinetics from birth through
8 adulthood (O’Flaherty, 1993, 1995).
- 9 • These models have been individually evaluated, to varying degrees, against empirical
10 physiological data on animals and humans and data on blood lead concentrations in
11 individuals and/or populations (U.S. Environmental Protection Agency, 1994a,b; Leggett,
12 1993; O’Flaherty, 1993). In evaluating models for use in risk assessment, exposure data
13 collected at hazardous waste sites have been used to drive some model simulations (Bowers
14 and Mattuck, 2001; Hogan et al., 1998). The exposure module in the IEUBK model makes
15 this type of evaluation feasible.
- 16 • Exposure-biokinetics models illustrate exposure-blood-body burden relationships and
17 provide a means for making predictions about these relationships that can be experimentally
18 or epidemiologically tested. The EPA IEUBK model for Pb has gained widespread use for
19 risk assessment purposes in the United States and is currently clearly the model of choice in
20 evaluating multimedia Pb exposure impacts on blood Pb levels and distribution of Pb to bone
21 and other tissues in young children <7 years old. The EPA All Ages Lead Model (AALM),
22 now under development, aims to extend beyond IEUBK capabilities to model external Pb
23 exposure impacts (including over many years) on internal Pb distribution not only in young
24 children, but also in older children, adolescents, young adults, and other adults well into older
25 years. The AALM essentially uses adaptations of IEUBK exposure module features, coupled
26 with adaptations of IEUBK biokinetics components (for young children) and of Leggett
27 model biokinetics components (for older children and adults). However, the AALM has not
28 yet undergone sufficient development and validation for its use yet beyond research and
29 validation purposes.

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32 **E.5 HEALTH EFFECTS ASSOCIATED WITH LEAD EXPOSURE**

33 Both epidemiologic and toxicologic studies have shown that environmentally relevant
34 levels of Pb affect many different organ systems. Research completed since the 1986
35 AQCD/Addendum and 1990 Supplement indicates that Pb effects occur at blood-Pb even lower
36 than those previously reported for many endpoints. Remarkable progress has been made since
37 the mid-1980s in understanding the Pb effects on health. Recent studies have focused on details
38 of the associations, including the shapes of concentration-response relationships, especially at
39 levels well within the range of general population exposures, and on those biological and/or

1 socioenvironmental factors that either increase or decrease an individual's risk. Key findings
2 and conclusions regarding important outcomes of newly available toxicologic and epidemiologic
3 studies of Pb health effects are highlighted below.

4

5 **Neurotoxic Effects of Pb Exposure**

- 6 • Neurobehavioral effects of Pb-exposure early in development (during fetal, neonatal, and
7 later postnatal periods) in young infants and children (≤ 7 years old) have been observed with
8 remarkable consistency across numerous studies involving varying study designs, different
9 developmental assessment protocols, and diverse populations. Negative Pb impacts on
10 neurocognitive ability and other neurobehavioral outcomes are robust in most recent studies
11 even after adjustment for numerous potentially confounding factors (including quality of care
12 giving, parental intelligence, and socioeconomic status). These effects generally appear to
13 persist into adolescence and young adulthood. However, experimental studies indicate that
14 environmental enrichment during development can partially mitigate the effects of Pb on
15 cognitive function.

- 16 • The overall weight of the available evidence provides clear substantiation of neurocognitive
17 decrements being associated in young children with blood-Pb concentrations in the range of
18 5-10 $\mu\text{g/dL}$, and possibly somewhat lower. Some newly available analyses appear to show
19 Pb effects on the intellectual attainment of preschool and school age children at population
20 mean blood-Pb levels ranging down to as low as 2 to 8 $\mu\text{g/dL}$. Also, a decline of 6.2 points
21 in full scale IQ for an increase in concurrent blood Pb levels from 1 to 10 $\mu\text{g/dL}$ has been
22 estimated, based on a pooled analysis of results derived from seven well-conducted
23 prospective epidemiologic studies internationally.

- 24 • In adults, neurotoxic Pb effects may not be as readily detected via neurobehavioral testing
25 due to cognitive reserve, i.e., the ability to compensate for brain impairment. There is no
26 clearly consistent evidence that environmental lead exposure is associated with impaired
27 cognitive performance in the elderly, if competing risk factors are considered.

- 28 • Animal toxicology data indicate that developmental Pb exposures creating steady-state
29 blood-Pb concentrations of $\sim 10 \mu\text{g/dL}$ result in behavioral impairments that persist into
30 adulthood in rats and monkeys. No evident threshold has yet been found; and Pb-induced
31 deficits, for the most part, have been found to be very persistent, even with various chelation
32 treatments. In rats, neurobehavioral deficits that persisted well into adulthood were observed
33 with prenatal, preweaning, and postweaning Pb exposure. In monkeys, such neurobehavioral
34 deficits were observed both with in utero-only exposure and with early postnatal-only
35 exposure when peak blood-Pb levels did not exceed 15 $\mu\text{g/dL}$ and steady-state levels were
36 $\sim 11 \mu\text{g/dL}$.

- 37 • Learning impairment has been observed in animal studies at blood levels as low as 10 $\mu\text{g/dL}$,
38 with higher level learning showing greater impairment than simple learning tasks. The
39 mechanisms associated with these deficits include: response perseveration; insensitivity to
40 changes in reinforcement density or contingencies; deficits in attention; reduced ability to
41 inhibit inappropriate responding; impulsivity; and distractibility.

- 1 • Lead affects reactivity to the environment and social behavior in both rodents and nonhuman
2 primates at blood lead levels of 15 to 40 µg/dL. Rodent studies show that Pb exposure
3 potentiates the effects of stress in females.
- 4 • Auditory function has also been shown to be impaired at blood lead levels of 33 µg/dL, while
5 visual functions are affected at 19 µg/dL.
- 6 • Neurotoxicological studies in animals clearly demonstrated that Pb mimics calcium and
7 affects neurotransmission and synaptic plasticity.
- 8 • Epidemiologic studies have identified genetic polymorphisms of two genes that may alter
9 susceptibility to the neurodevelopmental consequences of Pb exposure in children. Variant
10 alleles of the ALAD gene are associated with differences in absorption, retention, and
11 toxicokinetics of Pb. Polymorphisms of the vitamin D receptor gene have been shown to
12 affect the rate of resorption and excretion of Pb over time. These studies are only suggestive,
13 and parallel animal studies have not been completed.

14

15 **Cardiovascular Effects of Lead**

- 16 • Epidemiologic studies have consistently demonstrated associations between Pb exposure and
17 enhanced risk of deleterious cardiovascular outcomes, including increased blood pressure
18 and incidence of hypertension. Studies indicate that a doubling of blood-Pb level is
19 associated with a 1.0 mm Hg increase in systolic blood pressure and a 0.6 mm Hg increase in
20 diastolic pressure. Studies have also found that cumulative past lead exposure (e.g., bone
21 lead) may be as important, if not more, than present Pb exposure in assessing cardiovascular
22 effects. The evidence for an association of Pb with cardiovascular morbidity and mortality is
23 limited but supportive.
- 24 • Experimental toxicology studies have confirmed Pb effects on cardiovascular functions.
25 Most studies have shown that exposures creating blood-Pb levels of ~20 to 30 µg/dL for
26 extended periods resulted in arterial hypertension that persisted long after the cessation of Pb
27 exposure in genetically normal animals. One study reported blood pressure increases at
28 blood-Pb levels as low as 2 µg/dL in rats. A number of in vivo and in vitro studies provide
29 compelling evidence for the role of oxidative stress in the pathogenesis of Pb-induced
30 hypertension. However, experimental investigations into the cardiovascular effects of Pb in
31 animal studies are unclear as to why low, but not high, levels of Pb exposure cause
32 hypertension in experimental animals.

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34 **Renal Effects of Lead**

- 35 • In the general population, both circulating and cumulative Pb was found to be associated
36 with longitudinal decline in renal function. Effects on creatine clearance have been reported
37 in human adult hypertensives to be associated with general population mean blood-Pb levels
38 of only 4.2 µg/dL. The public health significance of such effects is not clear, however, in
39 view of more serious signs of kidney dysfunction being seen in occupationally exposed
40 workers only at much higher blood-Pb levels (>30-40 µg/dL).

- 1 • Experimental studies using laboratory animals demonstrated that the initial accumulation of
2 absorbed Pb occurs primarily in the kidneys. This takes place mainly through glomerular
3 filtration and subsequent reabsorption, and, to a small extent, through direct absorption from
4 the blood. Both low dose Pb-treated animals and high dose Pb-treated animals showed a
5 “hyperfiltration” phenomenon during the first 3 months of Pb exposure. Investigations into
6 biochemical alterations in Pb-induced renal toxicity suggested a role for oxidative stress and
7 involvement of NO, with a significant increase in nitrotyrosine and substantial fall in urinary
8 excretion of NO_x.
- 9 • Iron deficiency increases intestinal absorption of Pb and the Pb content of soft tissues and
10 bone. Aluminum decreases kidney Pb content and serum creatinine in Pb-intoxicated
11 animals. Age also has an effect on Pb retention. There is higher Pb retention at a very young
12 age and lower bone and kidney Pb at old age, attributed in part to increased bone resorption
13 and decreased bone accretion and, also, kidney Pb.

14 **Effects of Lead on the Immune System**

- 16 • Findings from recent epidemiologic studies suggest that Pb exposure may be associated with
17 effects on cellular and humoral immunity. These include changes in serum immunoglobulin
18 levels. Studies of biomarkers of humoral immunity in children have consistently found
19 significant associations between increasing blood-Pb concentrations and serum IgE levels at
20 blood-Pb levels <10 µg/dL.
- 21 • Toxicologic studies have shown that Pb targets immune cells, causing suppression of delayed
22 type hypersensitivity response, elevation of IgE, and modulation of macrophages into a
23 hyper-inflammatory phenotype. These types of changes can cause increased risk of atopy,
24 asthma, and some forms of autoimmunity and reduced resistance to some infectious diseases.
25 Lead exposure of embryos resulting in blood-Pb levels <10 µg/dL can produce persistent
26 later-life immunotoxicity.

27 **Effects of Lead on Heme Synthesis**

- 29 • Lead exposure has been associated with disruption of heme synthesis in both children and
30 adults. Increases in blood lead concentration of approximately 20–30 µg/dL are sufficient to
31 halve erythrocyte ALAD activity and sufficiently inhibit ferrochelatase to double erythrocyte
32 protoporphyrin levels.
- 33 • Toxicological studies demonstrated that Pb intoxication interferes with red blood cell (RBC)
34 survival and alters RBC mobility. Hematological parameters, such as mean corpuscular
35 volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration, are
36 also significantly decreased upon exposure to Pb. These effects are due to internalization of
37 Pb by RBC. The transport of Pb across the RBC membrane is energy-independent and
38 carrier-mediated; and the uptake of Pb appears to be mediated by an anion exchanger through
39 a vanadate-sensitive pathway.
- 40 • Erythrocyte ALAD activity ratio (ratio of activated/non activated enzyme activity) has been
41 shown to be a sensitive, dose-responsive measure of Pb exposure, regardless of the mode of

1 administration of Pb. Competitive enzyme kinetic analyses in RBCs from both humans and
2 Cynomolgus monkeys indicated similar inhibition profiles by Pb.

3 4 **Effects of Lead on Bones and Teeth**

- 5 • Experimental studies in animals demonstrate that Pb substitutes for calcium and is readily
6 taken up and stored in the bone and teeth of animals, potentially allowing bone cell function
7 to be compromised both directly and indirectly by exposure.
- 8 • Relatively short term exposure of mature animals to Pb does not result in significant growth
9 suppression. However, chronic Pb exposure during times of inadequate nutrition have been
10 shown to adversely influence bone growth, including decreased bone density, decreased
11 trabecular bone, and growth plates.
- 12 • Exposure of developing animals to Pb during gestation and the immediate postnatal period
13 has clearly been shown to significantly depress early bone growth in a dose-dependent
14 fashion, though this effect is not manifest below a certain threshold.
- 15 • Systemically, Pb has been shown to disrupt mineralization of bone during growth, to alter
16 calcium binding proteins, and to increase calcium and phosphorus concentration in the blood
17 stream, in addition to potentially altering bone cell differentiation and function by altering
18 plasma levels of growth hormone and calcitropic hormones such as vitamin D₃ [1,25-
19 (OH)₂D₃.
- 20 • Periods of extensive bone remodeling, such as occur during weight loss, advanced age,
21 altered metabolic state, and pregnancy and lactation are all associated with mobilization
22 of Pb stores from bone of animals.
- 23 • Numerous epidemiologic studies and, separately, animal studies (both post-eruptive Pb
24 exposure and pre- and perinatal Pb exposure studies) suggest that Pb is a caries-promoting
25 element. However, whether Pb incorporation into the enamel surface compromises the
26 integrity and resistance of the surface to dissolution, and ultimately increases risk of dental
27 decay, is unclear.
- 28 • Increased risk of dental caries has been associated with lead exposure in children and adults.
29 Lead effects on caries were observed in populations whose mean blood-Pb levels were less
30 than 10 µg/dL.

31 32 **Reproductive and Developmental Effects of Lead**

- 33 • Epidemiologic evidence suggests small associations between Pb exposure and male
34 reproductive outcomes, including perturbed semen quality and increased time to pregnancy.
35 There are no adequate epidemiologic data to evaluate associations between Pb exposure and
36 female fertility. Most studies have yielded no associations, or weak associations, of Pb
37 exposure with thyroid hormone status and male reproductive endocrine status in highly
38 exposed occupational populations.

- 1 • New toxicologic studies support earlier conclusions, presented in the 1986 Pb AQCD, that
2 (a) Pb can produce both temporary and persisting effects on male and female reproductive
3 function and development and (b) Pb disrupts endocrine function at multiple points along the
4 hypothalamic-pituitary-gonadal axis. Although there is evidence for a common mode of
5 action, consistent effects on circulating testosterone levels are not always observed in
6 Pb-exposed animals. Inconsistencies in reports of circulating testosterone levels complicate
7 derivation of a dose-response relationship for this endpoint.
- 8 • Lead-induced testicular damage (ultrastructural changes in testes of monkeys at blood-Pb
9 >35 to 40 µg/dL) and altered female sex hormone release, imprinting during early
10 development, and altered female fertility all suggest Pb-induced reproductive effects.
11 However, Pb exposure does not generally produce total sterility. Pre- and postnatal exposure
12 to Pb has been demonstrated to result in fetal mortality and produce a variety of sublethal
13 effects in the offspring. Many of the Pb-induced sublethal developmental effects occur at
14 maternal blood-Pb levels that do not result in clinical (overt) toxicity in the mothers.
15 Teratogenic effects resulting from Pb exposure reported in a few studies appear to be
16 confounded by maternal toxicity.

17 18 **Lead Effects on Other Organ Systems**

- 19 • Lead impacts the hypothalamic-pituitary-adrenal axis, elevating corticosterone levels and
20 altering stress responsivity. This may be a potential mechanism contributing to Pb-induced
21 hypertension, with further possible roles in the etiology of diabetes, obesity and other
22 disorders.
- 23 • Studies of hepatic enzyme levels in serum suggest that liver injury may be present in lead
24 workers; however, associations specifically with Pb exposures are not evident. Children
25 exposed to relatively high levels of lead (blood Pb >30 µg/dL) exhibit depressed levels of
26 circulating 1,25-dihydroxy vitamin D (1,25-OH-D). However, associations between serum
27 vitamin D status and blood Pb were not evident in a study of calcium-replete children who
28 had average lifetime blood-Pb concentrations <25 µg/dL.
- 29 • Field studies that evaluated hepatic enzyme levels in serum suggest that liver injury may be
30 present in lead workers; however, associations specifically with Pb exposures have not been
31 well established.
- 32 • Simultaneous induction of the activities of phase II drug metabolizing enzymes and
33 decreased phase I enzymes with a single exposure to Pb nitrate in rat liver suggest that Pb is
34 capable of causing biochemical phenotype similar to hepatic nodules.
- 35 • Newer studies examined the induction of GST-P at both transcriptional and translational
36 levels using in vitro systems and indicated a role for Pb-nitrate and Pb-acetate in the
37 induction process.
- 38 • Lead-induced alterations in cholesterol metabolism appear to be mediated by the induction of
39 several enzymes related to cholesterol metabolism and the decrease of 7 α-hydroxylase, a
40 cholesterol catabolizing enzyme. This regulation of cholesterol homeostasis is modulated by
41 changes in cytokine expression and related signaling.

- 1 • Newer experimental evidence suggests that Pb-induced alterations in liver heme metabolism
2 involve perturbations in ALAD activity, porphyrin metabolism, alterations in Transferrin
3 gene expression, and associated changes in iron metabolism.
- 4 • Gastrointestinal (G.I.) absorption of Pb is influenced by a variety of factors, including
5 chemical and physical forms of the element in ingested media, age at intake, and various
6 nutritional factors. The degeneration of intestinal mucosal epithelium leading to potential
7 malabsorption and alterations in the jejunal ultrastructure (possibly associated with distortion
8 of glycocalyx layer) have been reported in the intestine of Pb-exposed rats.
- 9 • Nutritional studies that varied Pb, Ca, and vitamin D levels in the diet have demonstrated
10 competition of Pb with Ca absorption. Supplementation with vitamin D has been reported to
11 enhance intestinal absorption of Ca and Pb. Physiological amounts of vitamin D, when
12 administered to vitamin D-deficient rats, resulted in elevated Pb and Ca levels. In the case of
13 severe Ca deficiency, Pb ingestion results in a marked decrease in serum 1,25 hydroxy
14 vitamin D.

15

16 **Genotoxic and Carcinogenic Effects of Lead**

- 17 • Epidemiologic studies of highly exposed occupational populations suggest a relationship
18 between lead and cancers of the lung and the stomach; however the evidence is limited by the
19 presence of various potential confounders, including metal coexposures (e.g., to arsenic,
20 cadmium), smoking, and dietary habits. The 2004 IARC review concluded that inorganic
21 lead compounds were a probable carcinogen (Group IIA), based on limited evidence in
22 humans and sufficient evidence in animals.
- 23 • Studies of genotoxicity consistently find associations of lead exposure with DNA damage
24 and micronuclei formation; however, the associations with the more established indicator of
25 cancer risk, chromosomal aberrations, are inconsistent.
- 26 • Pb is an animal carcinogen and extends our understanding of mechanisms involved to
27 include a role for metallothionein. Specifically, the recent data show that metallothionein
28 may participate in Pb inclusion bodies and, thus, serves to prevent or reduce Pb-induced
29 tumorigenesis.
- 30 • In vitro cell culture studies that evaluated the potential for Pb to transform rodent cells are
31 inconsistent, and careful study of a time course of exposure is necessary to determine
32 whether Pb actually induces transformation in cultured rodent cells. There is increased
33 evidence suggesting that Pb may be co-carcinogenic or promotes the carcinogenicity of other
34 compounds. Cell culture studies do support a possible epigenetic mechanism or co-
35 mutagenic effects.

36

37 **Lead-Binding Proteins**

- 38 • Proteins depending upon sulfur-containing side chains for maintaining conformity or activity
39 are vulnerable to inactivation by Pb, due to its strong sulfur-binding affinity.

- 1 • The enzyme, ALAD, a 280 kDa protein, is inducible and is the major Pb-binding protein
2 within the erythrocyte.
- 3 • The Pb-binding protein in rat kidney has been identified as a cleavage product of α -2
4 microglobulin. The low molecular weight Pb-binding proteins in human kidney have been
5 identified as thymosin β 4 (molecular weight 5 kDa) and acyl-CoA binding protein
6 (molecular weight 9 kDa). In human brain, Pb-binding proteins include thymosin β 4 and an
7 unidentified protein of 23 kDa.
- 8 • Animal toxicology studies with metallothionein-null mice demonstrated a possible role for
9 metallothionein as a renal Pb-binding protein.

10

11 **Human Population Groups at Special Risk and Potential Public Health Impacts**

- 12 • Children, in general and especially low SES (often including larger proportions of African-
13 American and Hispanic) children, have been well-documented as being at increased risk for
14 Pb exposure and Pb-induced adverse health effects. This is due to several factors, including
15 enhanced exposure to Pb via ingestion of soil-Pb and/or dust-Pb due to normal hand-to-
16 mouth activity and/or pica.
- 17 • Even children with low Pb exposure levels (having blood Pb of 5-10 μ g/dL or, possibly,
18 somewhat lower) are at notable risk, due to apparent non-linear dose-response relationships
19 between blood Pb and neurodevelopmental outcomes. It is hypothesized that initial
20 neurodevelopmental lesions occurring at blood-Pb levels <10 μ g/dL may disrupt different
21 developmental processes in the nervous system than more severe high level exposures.
- 22 • Adults with idiosyncratic exposures to Pb through occupations, hobbies, make-up use, glazed
23 pottery, native medicines, and other sources are at risk for Pb toxicity. Certain ethnic and
24 racial groups are known to have cultural practices that involve ingestion of Pb-containing
25 substances, e.g., ingestion of foods or beverages stored in Pb-glazed pottery or imported
26 canned food from countries that allow Pb-soldered cans.
- 27 • Cumulative past Pb exposure, measured by bone Pb, may be a better predictor of
28 cardiovascular effects than current blood-Pb levels. African-Americans are known to have
29 substantially higher baseline blood pressure than other ethnic groups, so Pb's impact on an
30 already higher baseline could indicate a greater susceptibility to Pb for this group.
- 31 • Effects on adults of low-level Pb exposures also include some renal effects (i.e., altered
32 creatinine clearance) at blood-Pb levels <5 μ g/dL. Lead exposure combined with other risk
33 factors, such as diabetes, hypertension, or chronic renal insufficiency may result in clinically-
34 relevant effects in individuals with two or more other risk factors.
- 35 • At least two genetic polymorphisms, of the ALAD and the vitamin D receptor gene, have
36 been suggested to play a role in susceptibility to Pb. In one study, African-American
37 children were found to have a higher incidence of being homozygous for alleles of the
38 vitamin D receptor gene thought to contribute to greater Pb blood levels. This work is

1 preliminary and further studies will be necessary to determine implications of genetic
2 differences that may make certain populations more susceptible to Pb exposure.

- 3 • What was considered “low” for Pb exposure levels in the 1980s is an order of magnitude
4 higher than the current mean level in the U.S. population, and current average blood-Pb
5 levels in U.S. populations remain perhaps as much as two orders of magnitude above pre-
6 industrial “natural” levels in humans. There is no level of Pb exposure that has yet been
7 clearly identified, with confidence, as being “risk free.” Some recent studies of Pb
8 neurotoxicity in infants have observed effects at population average blood-Pb levels of only
9 1 or 2 µg/dL; and some cardiovascular, renal, and immune outcomes have been reported at
10 blood-Pb levels below 5 µg/dL.
- 11 • Public health interventions have resulted in declines, over the last 25 years, of more than
12 90% in the mean blood-Pb level within all age and gender subgroups of the U.S. population,
13 substantially decreasing the numbers of individuals at likely risk for Pb-induced toxicities.
14 Nevertheless, estimates of the magnitude of potential public health impacts of Pb exposure
15 can be substantial for the U.S. population. For example, in estimating the effect of Pb
16 exposure on intelligence, it was projected that the fraction of individuals with an IQ >120
17 would decrease from ~9% with no Pb exposure to less than 3% at a blood-Pb level of
18 10 µg/dL. Also, the fraction of individuals with an IQ >130 points was estimated as being
19 likely to decrease from 2.25% to 0.5% with a blood-Pb level change from 0 to 10 µg/dL. In
20 addition, an estimate of hypertension-related risk for serious cardiovascular events (coronary
21 disease, stroke, peripheral artery disease, cardiac failure) indicates that a decrease in blood Pb
22 from 10 to 5 µg/dL could result in an annual decrease of 27 events per 100,000 women and
23 39 events per 100,000 men.

24

25

26 **E.6 ENVIRONMENTAL EFFECTS OF LEAD**

27 Chapter 7 assesses the environmental effects of Pb, including discussion, in particular,
28 of Pb effects on terrestrial and aquatic ecosystems and the methodological approaches used to
29 study such effects.

30

31 **E.6.1 Terrestrial Ecosystems**

32 **Methodologies Used in Terrestrial Ecosystem Research**

- 33 • Metal species found in environmental media are often diverse, and existing data suggest that
34 their bioavailability may be significantly influenced by site-specific variations.
- 35 • Many different analytical and chemical techniques have been used to characterize a metal's
36 speciation in various media. Perhaps the most important factor in selecting a technique is
37 that, when dealing with metal-contaminated media, one most often is looking for a
38 proverbial “needle in a haystack.” Therefore, the speciation technique must not only provide

1 the information outlined above, but it must also determine that information from a medium
2 that contains very little of the metal. For a Pb-contaminated soil, less than 1% (modally) of a
3 single species can be responsible for a bulk metal's concentration above an action level.

- 4 • Limited data are available on the particle-size of discrete Pb phases from multimedia
5 environments. Laboratory data have been supported by extensive epidemiologic evidence,
6 enforcing the importance of particle size.
- 7 • Matrix associations, such as liberated versus enclosed, can play an important part in
8 bioavailability. For example, two different media with similar total Pb concentrations and Pb
9 forms (slag, Pb-oxide, and Pb-arsenate) can exhibit significantly different bioavailabilities.
- 10 • The biotic ligand model (BLM) is an equilibrium-based model that has been incorporated
11 into regulatory agencies guidelines (including the EPA) to predict effects of metals primarily
12 on aquatic biota and to aid in the understanding of their interactions with biological surfaces.
13 Currently, there is no acute BLM for Pb. Because of assumed similarities in mechanisms of
14 toxicity between aquatic and terrestrial organisms, it is likely that the BLM approach as
15 developed for the aquatic compartment may also be applicable to the terrestrial environment.
- 16 • In situ methodologies have been developed to lower soil-Pb relative bioavailability. To date,
17 the most common methods studied include the addition of soil amendments to either lower
18 the solubility of the Pb form or to provide sorbtion sites for fixation of pore-water Pb. These
19 amendments typically fall within the categories of phosphate, biosolid, and Al/Fe/Mn-oxide
20 amendments. Some of the drawbacks to soil amendment include phosphate toxicity to plants
21 and increased arsenic mobility at high soil phosphate concentrations. The use of iron(III)
22 phosphate seems to mitigate arsenic mobility, however increased concentrations of phosphate
23 and iron limit their application when drinking water quality is a concern.

24 25 **Distribution of Atmospherically Delivered Lead in Terrestrial Ecosystems**

- 26 • At the time of the publication of the 1986 Pb AQCD, the primary source of atmospheric Pb
27 was combustion of leaded gasoline. Lead in the atmosphere today, however, is not primarily
28 from gasoline consumption, but results largely from waste incineration, metal smelting, metal
29 production, and coal-fired power plants.
- 30 • Total Pb deposition during the 20th century has been estimated at 1 to 3 g Pb m⁻², depending
31 on elevation and proximity to urban areas. Total contemporary loadings to terrestrial
32 ecosystems are ~1 to 2 mg m⁻² year⁻¹. This is a relatively small annual flux of Pb compared
33 to the reservoir of ~0.5 to 4 g m⁻² of gasoline additive-derived Pb already deposited in
34 surface soils over much of the United States.
- 35 • Researchers have estimated that dry deposition accounts for anywhere between 10 to >90%
36 of total Pb deposition. Arid environments appear to have a much higher fraction of dry
37 deposition:total deposition. Furthermore, it is possible that Clean Air Act Legislation
38 enacted in the late 1970s preferentially reduced Pb associated with fine particles, so the
39 relative contributions of dry deposition may have changed in the last few decades.

- 1 • Although inputs of Pb to ecosystems are currently low, Pb export from watersheds via
2 groundwater and streams is substantially lower. Therefore, even at current input levels,
3 watersheds are accumulating anthropogenic Pb.
- 4 • Species of Pb delivered to terrestrial ecosystems can be inferred by emission source. For
5 example, Pb species emitted from automobile exhaust are dominated by particulate Pb
6 halides and double salts with ammonium halides (e.g., PbBrCl , $\text{PbBrCl}_2\text{NH}_4\text{Cl}$), while Pb
7 emitted from smelters is dominated by Pb-sulfur species. Halides from automobile exhaust
8 break down rapidly in the atmosphere, via redox reactions in the presence of atmospheric
9 acids. Lead phases in the atmosphere, and presumably the compounds delivered to the
10 surface of the earth (i.e., to vegetation and soils), are suspected to be in the form of PbSO_4 ,
11 PbS , and PbO .
- 12 • The importance of humic and fulvic acids and hydrous Mn- and Fe-oxides for scavenging Pb
13 in soils was discussed in some detail in the 1986 Pb AQCD. The importance of these Pb
14 binding substrates is reinforced by studies reported in the more contemporary literature.
- 15 • The amount of Pb that has leached into mineral soil appears to be on the order of 20 to 50%
16 of the total anthropogenic Pb deposition.
- 17 • The vertical distribution and mobility of atmospheric Pb in soils was poorly documented
18 prior to 1986. Techniques using radiogenic Pb isotopes had been developed to discern
19 between gasoline-derived Pb and natural, geogenic (native) Pb. These techniques provide
20 more accurate determinations of the depth-distribution and potential migration velocities for
21 atmospherically delivered Pb in soils.
- 22 • Selective chemical extractions have been used extensively over the past 20 years to quantify
23 amounts of a particular metal phase (e.g., PbS , Pb-humate, Pb-Fe/Mn-oxide) in soil or
24 sediment rather than total metal concentration. However, some problems persist with the
25 selective extraction technique: (a) extractions are rarely specific to a single phase; and (b) in
26 addition to the nonselectivity of reagents, significant metal redistribution has been found to
27 occur during sequential chemical extractions. Thus, although chemical extractions provide
28 some useful information on metal phases in soil or sediment, the results should be treated as
29 “operationally defined,” e.g., “ H_2O_2 -liberated Pb” rather than “organic Pb.”
- 30 • Soil solution dissolved organic matter content and pH typically have very strong positive and
31 negative correlations, respectively, with the concentration of dissolved Pb species.

32

33 **Terrestrial Species Response/Mode of Action**

- 34 • Plants take up Pb via their foliage and through their root systems. Surface deposition of Pb
35 onto plants may represent a significant contribution to the total Pb in and on the plant, as has
36 been observed for plants near smelters and along roadsides.
- 37 • There are two possible mechanisms (symplastic or apoplastic) by which Pb may enter the
38 root of a plant. The symplastic route is through the cell membranes of root hairs; this is the
39 mechanism of uptake for water and nutrients. The apoplastic route is an extracellular route

1 between epidermal cells into the intercellular spaces of the root cortex. The symplastic route
2 is considered the primary mechanism of Pb uptake in plants.

- 3 • Recent work supports previous conclusions that the form of metal tested, and its speciation in
4 soil, influence uptake and toxicity to plants and invertebrates. The oxide form of Pb is less
5 toxic than the chloride or acetate forms, which are less toxic than the nitrate form of Pb.
6 However, these results must be interpreted with caution, as the counterion (e.g., the nitrate
7 ion) may also be contributing to the observed toxicity.

- 8 • Lead may be detoxified in plants by deposition in root cell walls, and this may be influenced
9 by calcium concentrations. Other hypotheses put forward recently include the presence of
10 sulfur ligands and the sequestration of Pb in old leaves as detoxification mechanisms. Lead
11 detoxification has not been studied extensively in invertebrates. Glutathione detoxification
12 enzymes were measured in two species of spider. Lead may be stored in waste nodules in
13 earthworms or as pyromorphite in the nematode.

- 14 • Lead effects on heme synthesis (as measured primarily by ALAD activity and protoporphyrin
15 concentration) were documented in the 1986 Pb AQCD and continue to be studied.
16 However, researchers caution that changes in ALAD and other enzyme parameters are not
17 always related to adverse effects, but may simply indicate exposure. Other effects on plasma
18 enzymes, which may damage other organs, have been reported. Lead also may cause lipid
19 peroxidation, which may be alleviated by vitamin E, although Pb poisoning may still result.
20 Changes in fatty acid production have been reported, which may influence immune response
21 and bone formation.

- 22 • Insectivorous mammals may be more exposed to Pb than herbivores, and higher trophic-level
23 consumers may be less exposed than lower trophic-level organisms. Nutritionally-deficient
24 diets (including low calcium) cause increased uptake of Pb and greater toxicity in birds.

- 25 • Interactions of Pb with other metals are inconsistent, depending on the endpoint measured,
26 the tissue analyzed, the animal species, and the metal combination.

27 **Exposure/Response of Terrestrial Species**

- 29 • Recent critical advancements reported in the current Pb AQCD in understanding toxicity
30 levels relies heavily on the work completed by a multi-stakeholder group, consisting of
31 federal, state, consulting, industry, and academic participants, led by the EPA to develop
32 Ecological Soil Screening Levels (Eco-SSLs).

- 33 • Eco-SSLs are concentrations of contaminants in soils that would result in little or no
34 measureable effect on ecological receptors. They were developed following rigorous
35 scientific protocols and were subjected to two rounds of peer review. The Eco-SSLs for
36 terrestrial plants, birds, mammals, and soil invertebrates are 120, 11, 56, and 1700 mg Pb/kg
37 soil, respectively.

1 **Effects of Lead on Natural Terrestrial Ecosystems**

- 2 • Atmospheric Pb pollution has resulted in the accumulation of Pb in terrestrial ecosystems
3 throughout the world. In the United States, pollutant Pb represents a significant fraction of
4 the total Pb burden in soils, even in sites remote from smelters and other industrial plants.
5 However, few significant effects of Pb pollution have been observed at sites that are not near
6 point sources of Pb.
- 7 • Evidence from precipitation collection and sediment analyses indicates that atmospheric
8 deposition of Pb has declined dramatically (>95%) at sites unaffected by point sources of Pb,
9 and there is little evidence that Pb accumulated in soils at these sites represents a threat to
10 ground water or surface water supplies.
- 11 • The highest environmental risk for Pb in terrestrial ecosystems exists at sites within about
12 50 km of smelters and other Pb-emitting industrial sites. Assessing the risks specifically
13 associated with Pb is difficult, because these sites also experience elevated concentrations of
14 other metals and because of effects related to SO₂ emissions. The concentrations of Pb in
15 soils, vegetation, and fauna at these sites can be two to three orders of magnitude higher than
16 in reference areas.
- 17 • In the most extreme cases, near smelter sites, the death of vegetation causes a near-complete
18 collapse of the detrital food web, creating a terrestrial ecosystem in which energy and
19 nutrient flows are minimal.
- 20 • More commonly, stress in soil microorganisms and detritivores can cause reductions in the
21 rate of decomposition of detrital organic matter. Although there is little evidence of
22 significant bioaccumulation of Pb in natural terrestrial ecosystems, reductions in microbial
23 and detritivorous populations can affect the success of their predators. Thus, at present,
24 industrial point sources represent the greatest Pb-related threat to the maintenance of
25 sustainable, healthy, diverse, and high-functioning terrestrial ecosystems in the United States.

26

27 **AQUATIC ECOSYSTEMS**

28 **Methodologies Used in Aquatic Ecosystem Research**

- 29 • Many of the terrestrial methods can also be applied to suspended solids and sediments
30 collected from aquatic ecosystems. Just as in the terrestrial environment, the speciation of Pb
31 and other trace metals in natural freshwaters and seawater plays a crucial role in determining
32 their reactivity, mobility, bioavailability, and toxicity. Many of the same speciation
33 techniques employed for the speciation of Pb in terrestrial ecosystems are applicable in
34 aquatic ecosystems.
- 35 • There is now a better understanding of the potential effects of sampling, sample handling,
36 and sample preparation on aqueous-phase metal speciation. Thus, a need has arisen for
37 dynamic analytical techniques that are able to capture a metal's speciation, in-situ and in real
38 time.

- 1 • With few exceptions, ambient water quality criteria (AWQC) are derived based on data from
2 aquatic toxicity studies conducted in the laboratory. In general, both acute (short term) and
3 chronic (long term) AWQCs are developed. Depending on the species, the toxicity studies
4 considered for developing acute criteria range in length from 48 to 96 hours.
- 5 • Acceptable chronic toxicity studies should encompass the full life cycle of the test organism,
6 although for fish, early life stage or partial life cycle toxicity studies are considered
7 acceptable. Acceptable endpoints include reproduction, growth and development, and
8 survival, with the effect levels expressed as the chronic value.
- 9 • The biotic ligand model (BLM) is gaining application in aquatic toxicity testing. Unlike
10 earlier metal toxicity models, the BLM uses the biotic ligand, rather than the fish gill as the
11 site of toxic action. This approach, therefore, considers that the external fish gill surface
12 contains receptor sites for metal binding and that acute toxicity is associated with the binding
13 of metals to defined sites (biotic ligands) on or within the organism. Work is being done to
14 incorporate into the model dietary uptake of metals, a very important and often overlooked
15 aspect of bioavailability.

16

17 **Distribution of Lead in Aquatic Ecosystems**

- 18 • Atmospheric Pb is delivered to aquatic ecosystems primarily through deposition (wet and/or
19 dry) or through erosional transport of soil particles.
- 20 • A significant portion of Pb in the aquatic environment exists in the undissolved form (i.e.,
21 bound to suspended particulate matter). The ratio of Pb in suspended solids to Pb in filtrate
22 varies from 4:1 in rural streams to 27:1 in urban streams.
- 23 • The oxidation potential of Pb is high in slightly acidic solutions, and Pb^{2+} binds with high
24 affinity to sulfur-, oxygen-, and nitrogen-containing ligands. Therefore, speciation of Pb in
25 the aquatic environment is controlled by many factors (e.g., pH, redox, dissolved organic
26 carbon, sulfides). The primary form of Pb in aquatic environments is divalent (Pb^{2+}), while
27 Pb^{4+} exists only under extreme oxidizing conditions. Labile forms of Pb (e.g., Pb^{2+} , $PbOH^+$,
28 $PbCO_3$) are a significant portion of the Pb inputs to aquatic systems from atmospheric
29 washout. Lead is typically present in acidic aquatic environments as $PbSO_4$, $PbCl_4$, ionic Pb,
30 cationic forms of Pb-hydroxide, and ordinary Pb-hydroxide ($Pb(OH)_2$). In alkaline waters,
31 common species of Pb include anionic forms of Pb-carbonate ($Pb(CO_3)$) and $Pb(OH)_2$.
- 32 • Lead concentrations in lakes and oceans were generally found to be much lower than those
33 measured in the lotic waters assessed by NAWQA.
- 34 • Based on a synthesis of NAWQA data from the United States, Pb concentrations in surface
35 waters, sediments, and fish tissues range from 0.04 to 30 $\mu\text{g/L}$, 0.5 to 12,000 mg/kg, and
36 0.08 to 23 mg/kg, respectively.

37

1 **Aquatic Species Response/Mode of Action**

- 2 • Recent research has suggested that due to the low solubility of Pb in water, dietary Pb (i.e.,
3 lead adsorbed to sediment, particulate matter, and food) may contribute substantially to
4 exposure and toxicity in aquatic biota.
- 5 • Generally speaking, aquatic organisms exhibit three Pb accumulation strategies:
6 (1) accumulation of significant Pb concentrations with a low rate of loss, (2) excretion of
7 Pb roughly in balance with availability of metal in the environment, and (3) weak net
8 accumulation due to very low metal uptake rate and no significant excretion.
- 9 • Protists and plants produce intracellular polypeptides that form complexes with Pb.
10 Macrophytes and wetland plants that thrive in Pb-contaminated regions have developed
11 translocation strategies for tolerance and detoxification.
- 12 • Like aquatic plants and protists, aquatic animals detoxify Pb by preventing it from being
13 metabolically available, though their mechanisms for doing so vary. Invertebrates use
14 lysosomal-vacuolar systems to sequester and process Pb within glandular cells. They also
15 accumulate Pb as deposits on and within skeletal tissue, and some can efficiently excrete Pb.
16 Fish scales and mucous chelate Pb in the water column, and potentially reduce visceral
17 exposure.
- 18 • Numerous studies have reported the effects of Pb exposure on blood chemistry in aquatic
19 biota. Plasma cholesterol, blood serum protein, albumin, and globulin concentrations were
20 identified as bioindicators of Pb stress in fish.
- 21 • Nutrients affect Pb toxicity in aquatic organisms. Some nutrients seem capable of reducing
22 toxicity. Exposure to Pb has not been shown to reduce nutrient uptake ability, though it has
23 been demonstrated that Pb exposure may lead to increased production and loss of organic
24 material (e.g., mucus and other complex organic ligands).
- 25 • The two most commonly reported Pb-element interactions are between Pb and calcium and
26 between Pb and zinc. Both calcium and zinc are essential elements in organisms and the
27 interaction of Pb with these ions can lead to adverse effects both by increased Pb uptake
28 and by a decrease in Ca and Zn required for normal metabolic functions.

29
30 **Exposure/Response of Aquatic Species**

- 31 • The 1986 Pb AQCD reviewed data in the context of sublethal effects of Pb exposure. The
32 document focused on describing the types and ranges of Pb exposures in ecosystems likely to
33 adversely impact domestic animals. As such, the 1986 AQCD did not provide a
34 comprehensive analysis of the effects of Pb to most aquatic primary producers, consumers,
35 and decomposers.
- 36 • Waterborne Pb is highly toxic to aquatic organisms, with toxicity varying with the species
37 and life stage tested, duration of exposure, form of Pb tested, and water quality
38 characteristics.

- 1 • Among the species tested, aquatic invertebrates, such as amphipods and water fleas, were the
2 most sensitive to the effects of Pb, with adverse effects being reported at concentrations
3 ranging from 0.45 to 8000 µg/L.
- 4 • Freshwater fish demonstrated adverse effects at concentrations ranging from 10 to
5 >5400 µg/L, depending generally upon water quality parameters.
- 6 • Amphibians tend to be relatively Pb tolerant; however, they may exhibit decreased enzyme
7 activity (e.g., ALAD reduction) and changes in behavior (e.g., hypoxia response behavior).

8

9 **Effects of Lead on Natural Aquatic Ecosystems**

- 10 • Natural systems frequently contain multiple metals, making it difficult to attribute observed
11 adverse effects to single metals. For example, macroinvertebrate communities have been
12 widely studied with respect to metals contamination and community composition and species
13 richness. In these studies, multiple metals were evaluated and correlations between observed
14 community level effects were ascertained. The results often indicate a correlation between
15 the presence of one or more metals (or total metals) and the negative effects observed.
16 While, correlation may imply a relationship between two variables, it does not imply
17 causation of effects.
- 18 • In simulated microcosms or natural systems, environmental exposure to Pb in water and
19 sediment has been shown to affect energy flow and nutrient cycling and benthic community
20 structure.
- 21 • In field studies, Pb contamination has been shown to significantly alter the aquatic
22 environment through bioaccumulation and alterations of community structure and function.
- 23 • Exposure to Pb in laboratory studies and simulated ecosystems may alter species competitive
24 behaviors, predator-prey interactions, and contaminant avoidance behaviors. Alteration of
25 these interactions may have negative effects on species abundance and community structure.
- 26 • In natural aquatic ecosystems, Pb is often found coexisting with other metals and other
27 stressors. Thus, understanding the effects of Pb in natural systems is challenging given that
28 observed effects may be due to cumulative toxicity from multiple stressors.

29

30 **CRITICAL LOADS FOR LEAD IN TERRESTRIAL AND** 31 **AQUATIC ECOSYSTEMS**

- 32 • Critical loads are defined as threshold deposition rates of air pollutants that current
33 knowledge indicates will not cause long-term adverse effects to ecosystem structure and
34 function. A critical load is related to an ecosystem's sensitivity to anthropogenic inputs of a
35 specific chemical.
- 36 • The critical loads approach for sensitive ecosystems from acidification has been in use
37 throughout Europe for about 20 years. Its application to Pb and other heavy metals is more

1 recent. To date, the critical loads framework has not been used for regulatory purposes in the
2 United States for any chemical.

- 3 • Speciation strongly influences the toxicity of Pb in soil and water and partitioning between
4 dissolved and solid phases determines the concentration of Pb in soil drainage water, but it
5 has not been taken into account in most of the critical load calculations for Pb performed to
6 date.
- 7 • Runoff of Pb from soil may be the major source of Pb into aquatic systems. However, little
8 attempt has been made to include this source into critical load calculations for aquatic
9 systems due to the complexity of including this source in the critical load models.