Integrated Review Plan for the National Ambient Air Quality Standards for Lead.

Volume 3: Planning Document for Quantitative Exposure/Risk Analyses

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U.S. Environmental Protection Agency

Office of Air Quality Planning and Standards
Health and Environmental Impacts Division

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PREFACE

The planning phase of the U.S. Environmental Protection Agency's (EPA's) reviews of the national ambient air quality standards (NAAQS) includes development of an integrated review plan (IRP) which is made available for public comment and provided to the Clean Air Scientific Advisory Committee (CASAC) for review or consultation. As a result of recent efforts to improve the efficiency of the planning phase and to facilitate the receipt of timely input from the CASAC and the public, the IRP for the current review of the lead NAAQS is comprised of three volumes. Volume 1 provides background information on the air quality criteria and standards for lead, and may serve as a reference for the public and the CASAC in their consideration of the subsequent two volumes. Volume 2 addresses the general approach for the review and planning for the integrated science assessment (ISA) and was the subject of a consultation with the CASAC in 2022. Volume 3 (this document) is the planning document for quantitative analyses to be considered in the policy assessment (PA), including exposure and risk analyses, and will be the subject of a consultation with the CASAC in 2023. It will describe key considerations in EPA's development of the PA and planning with regard to any quantitative exposure/risk analyses to inform the review. In order that consideration of the availability of new evidence in the review can inform these plans, the development and public availability of Volume 3 has generally coincided with that of the draft ISA.

1 INTRODUCTION/BACKGROUND

The U.S. Environmental Protection Agency (EPA) is conducting a review of the air quality criteria and the national ambient air quality standards (NAAQS) for lead (Pb). Plans for the review have been described in Volumes I and II of the Integrated Review Plan for this review (U.S. EPA, 2022a, b; hereafter referred to as the IRP, volumes 1 and 2). This third volume (titled *Integrated Review Plan for the Lead National Ambient Air Quality Standards, 3. Planning Document for Quantitative Exposure/Risk Analyses* – hereafter referred to as the IRP, volume 3) is the planning document for quantitative analyses to be considered in the policy assessment (PA), including exposure and risk analyses. It describes key considerations in planning for any quantitative exposure/risk analyses to inform the review. The purpose of this planning document is to describe the consideration of the extent to which newly available scientific evidence and tools or methodologies warrant the conduct of quantitative risk and exposure analyses that might inform this review, and as warranted, the initial planning for such analyses. Also considered is the extent to which newly available evidence may refine our characterization of exposure and risk estimates available in the last review.

The current review of the Pb air quality criteria and standards builds on the substantial body of work done during the course of prior reviews, represented both in comprehensive science assessments (e.g., U.S. EPA, 2006a [2006 AQCD]; U.S. EPA, 2013a [2013 ISA]) and past quantitative exposure and risk analyses.[1] These different types of information, evaluated in past policy assessments, provided the basis for decisions on the existing Pb NAAQS. This planning document presents a critical evaluation of information related to Pb human and ecological exposure and risk (e.g., data, modeling approaches) newly available in this review as identified in the first draft *Integrated Science Assessment for Lead* (draft ISA; U.S. EPA, 2023a). The focus of this evaluation is consideration of the risk and exposure analyses for health and ecological risk warranted by the newly available evidence.

This document is intended to facilitate consultation with the Clean Air Scientific Advisory Committee (CASAC), as well as public review, for the purpose of obtaining advice on EPA's consideration of the recently available evidence (information, methods, etc.) as it relates to its potential impact on quantitative exposure and risk analyses, both with regard to consideration of the extent to which new assessments are warranted in this review and with

[1] For example, in the 2008 review, EPA staff designed and conducted a complex multimedia, multipathway health risk assessment involving case studies representing different ambient air Pb exposure circumstances, and an assessment of the available information on ecological impacts of Pb, including the consideration of potentially vulnerable ecosystems.

regard to our consideration of prior assessments in evaluating risk and exposure-related considerations in our Policy Assessment for this review. The discussion in this document is intended to build upon the exposure and risk assessment approaches employed in past reviews, and on Agency experience with Pb exposure and risk assessment since that time, while also drawing from information presented in the March 2023 draft of the ISA for the current review.

Legislative Requirements

Sections 108 and 109 of the Clean Air Act (Act) govern the establishment and periodic review of the NAAQS. These standards are established for pollutants that may reasonably be anticipated to endanger public health and welfare, and whose presence in the ambient air results from numerous or diverse mobile or stationary sources. The NAAQS are to be based on air quality criteria, which are to accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare which may be expected from the presence of the pollutant in ambient air. The EPA Administrator is to promulgate and periodically review, at five-year intervals, "primary" (health-based) and "secondary" (welfare-based)[1] NAAQS for such pollutants.[1] Based on periodic reviews of the air quality criteria and standards, the Administrator is to make revisions in the criteria and standards, and promulgate any new standards, as may be appropriate. The Act also requires that an independent scientific review committee advise the Administrator as part of this NAAQS review process, a function now performed by the CASAC.

[1] The legislative history of section 109 indicates that a primary standard is to be set at "the maximum permissible ambient air level … which will protect the health of any [sensitive] group of the population," and that for this purpose "reference should be made to a representative sample of persons comprising the sensitive group rather than to a single person in such a group." S. Rep. No. 91–1196, 91st Cong., 2d Sess. 10 (1970).

[2] Under CAA section 302(h) (42 U.S.C. § 7602(h)), effects on welfare include, but are not limited to, "effects on soils, water, crops, vegetation, manmade materials, animals, wildlife, weather, visibility, and climate, damage to and deterioration of property, and hazards to transportation, as well as effects on economic values and on personal comfort and well-being."

Additional background on this Pb NAAQS review is presented in the IRP, volume 1. That document describes the preparation of key documents in the NAAQS review process including an ISA and a PA. The ISA provides a critical assessment of the latest available scientific information upon which the NAAQS are to be based, and the PA evaluates the policy implications of the information contained in the ISA and of any policy-relevant quantitative analyses, such as quantitative human and/or ecological risk and exposure assessments, that were performed for the review or for past reviews. Based on this evaluation, the PA presents staff conclusions regarding standard-setting options for the Administrator to consider in reaching decisions on the NAAQS.[2]

1.1 CURRENT REVIEW OF AIR QUALITY CRITERIA AND STANDARDS FOR LEAD

In July 2020, EPA announced the initiation of the current periodic review of the air quality criteria for Pb and the Pb NAAQS and issued a call for information in the *Federal Register* (85 FR 40641, July 7, 2020). Volumes 1 and 2 of the IRP were released in March 2022 (U.S. EPA, 2022a,b). The former provides background on the Pb NAAQS, and the latter is the planning document for the review and the ISA. Volume 2 was the subject of a consultation with CASAC on April 8, 2022 (87 FR 15985, March 21, 2022; Shepard, 2022). With consideration of input received during this consultation, EPA has separately developed a draft ISA, released on March 31, 2023, for public comment and CASAC review (88 FR 19302, March 31, 2023).

With consideration of the newly available evidence identified in the draft ISA, the EPA has developed this planning document for quantitative analyses, including exposure/risk analyses, that might be warranted to inform decisions in the current review. This planning document comprises the third volume of the IRP. With consideration of the CASAC review of the draft ISA and consultation discussions on volumes 2 and 3 of the IRP, the EPA will develop a draft of the PA (with associated policy evaluations and quantitative analyses) for public and CASAC review. The current timeline projected for completing this Pb NAAQS review is presented in Table 1-1. Completion of the final ISA and PA are projected in Spring 2024 and Fall 2024, respectively. These will be followed by proposed and final decisions for the review, projected in 2025 and 2026, respectively.

[2] Decisions on the NAAQS involve consideration of the four basic elements of a standard: indicator, averaging time, form, and level. The indicator defines the pollutant to be measured in the ambient air for the purpose of determining compliance with the standard. The averaging time defines the time period over which air quality measurements are to be obtained and averaged, considering evidence of effects associated with various time periods of exposure. The form of a standard defines the air quality statistic that is to be compared to the level of the standard in determining whether an area attains the standard.

Table 1-1. Schedule for the review of ambient air quality criteria and NAAQS for Pb.

Stage of Review	Major Milestone	Target Dates
Planning	Federal Register Call for Information	July 7, 2020
	Integrated Review Plan (IRP), volumes 1 and 2	March 2022
	CASAC consultation on IRP, volume 2	April 2022
	IRP, volume 3	May 2023
	CASAC consultation on IRP, volume 3	June 2023
Science Assessment	External review draft of ISA	March 2023
	CASAC public meeting for review of draft ISA	June 2023
	Final ISA	Spring 2024
Quantitative Exposure/Risk Analyses and Policy Assessment	External review draft of PA (including quantitative air quality, exposure and/or risk analyses, as warranted)	Winter 2023/24
	CASAC public meeting for review of draft PA	2024
	Final PA	Fall 2024
Regulatory Process	Notice of proposed decision	2025
	Notice of final decision	2026

1.2 MULTIMEDIA, MULTISOURCE ASPECTS OF ENVIRONMENTAL LEAD AND POPULATION EXPOSURE

Unlike most other pollutants for which NAAQS are established, Pb is a multimedia, multisource pollutant. Other sources of Pb in the environment include surface water discharges, industrial and other historically contaminated sites, as well as Pb associated with past uses of Pb-based paint. Other sources of Pb to human exposures include plumbing that includes Pb solder or piping, as well as some imported dietary items and consumer products (draft ISA, Appendix 2). While such exposures remain today, exposures related to many nonair sources that occurred in the past, such as from the use of Pb solder in canned foods, have been dramatically reduced or eliminated for today's populations (2013 ISA, section 3.1).

Lead emitted into ambient air may subsequently occur in multiple environmental media, contributing to multiple pathways of exposure for humans and ecological receptors. This multimedia distribution of, and multipathway exposure to, air-related Pb has a key role in the Agency's consideration of the Pb NAAQS. Lead emitted into the air is predominantly in particulate form, which can be transported long or short distances depending on particle size. Exposure to Pb emitted into the ambient air (air-related Pb) can occur directly by inhalation or indirectly by ingestion of Pb-contaminated food, water or other materials including dust and soil. These exposures occur as Pb emitted into the ambient air is distributed to other environmental media and can contribute to human exposures via indoor and outdoor dusts, outdoor soil, food

and drinking water, as well as inhalation of air. Air-related exposure pathways are affected by changes to air quality, including changes in concentrations of Pb in air and changes in atmospheric deposition of Pb. Further, because of its persistence in the environment, Pb deposited from the air may contribute to human and ecological exposures for years into the future. Thus, the roles of both air concentration and air deposition in human exposure pathways, and the persistence of Pb once deposited, influence the dynamics of the response of the various Pb exposure pathways to changes in air quality.

1.3 TEMPORAL TRENDS IN EMISSIONS, AMBIENT AIR CONCENTRATIONS AND POPULATION BLOOD LEAD

As background for the subsequent chapters, this section presents trends in air Pb emissions and concentrations (section 1.3.1) and trends in population blood Pb concentrations (section 1.3.2). Section 1.3.2 also summarizes patterns of blood Pb concentrations across demographic groups, and estimates of the appreciable difference in Pb exposure history experienced by population cohorts born at different times in the past.

1.3.1 Air Pb Emissions and Concentrations

Air Pb emissions have decreased substantially over the past 50 years, with the most dramatic reductions occurring between 1970 and 1995 due to the removal of Pb from gasoline used in highway vehicles (2014 PA, Figure 2-1). For example, total air Pb emissions in the U.S. are estimated to have declined from over 200,000 tpy in 1970 to approximately 5,000 tpy in 1990. Lead emissions have continued to decrease since 1990 (Figure 1-1), with significant reductions occurring in the metals industries as a result of national emissions standards for hazardous air pollutants.

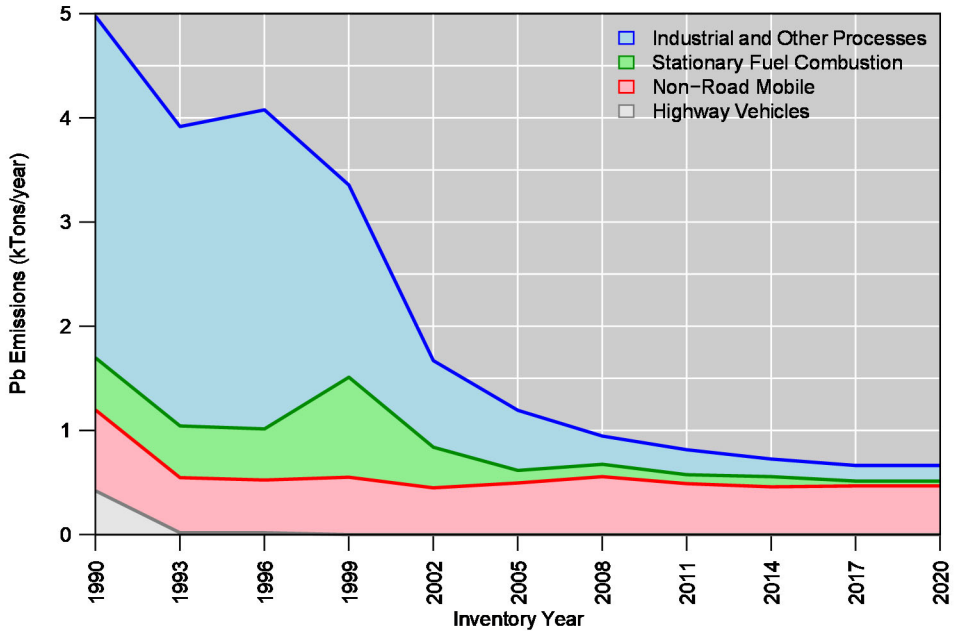


Figure 1-1. Long-term trends in air Pb emissions (U.S. EPA, 2023b).

In response to reductions in air emissions, air Pb concentrations have also declined over the past three to four decades. For example, as reported in the 2013 Pb ISA, from 1980 to 2010 the national median of maximum 3-month average Pb concentrations of 74 Pb-TSP monitors in the U.S. declined from 0.87 μg/m^3 in 1980 to 0.03 μg/m^3 in 2010, as a result of the phase-out of leaded gasoline for automobiles and reductions of industrial use and processing of Pb (2013 ISA, section 1.2.2). Although many of the network monitors on which these observations are based are sited near major industrial sources, the 2013 Pb ISA also documented a strong decreasing trend in ambient air Pb concentrations from five monitors in the vicinity of major roadways in urban areas. The average of Pb-TSP concentrations from these monitors dropped from 0.90 μg/m^3 in 1980 to 0.18 μg/m^3 in 1986 to 0.01 μg/m^3 by 2010 (2013 ISA, section 2.5.1.2; 2014 PA, section 2.2.2.1). Air Pb concentrations have continued to decline since 2010 (draft ISA, Appendix 1, section 1.5.1). These long-term national trends are generally reflected in long-term local and regional observations of Pb concentrations in the U.S. and Canada for diverse locations and conditions (draft ISA, Appendix 1, section 1.5.1).

1.3.2 Human Exposure and Population Blood Pb Concentrations

As described in the 2013 ISA and prior AQCDs, blood Pb is a commonly used exposure metric that reflects human exposures across all routes and pathways. Upon absorption into the body (via gastrointestinal tract or alveoli of the lungs, depending on pathway), individuals' multimedia Pb exposures are reflected in the blood. The bloodstream provides distribution of Pb to organs throughout the body with vast majority of Pb accumulating in bone which serves as a

long-term storage depot over a person's lifetime. Thus, bone Pb is another metric of exposure (that is less easily monitored in a population). During times of physiological changes, certain disease states and lifestages, such as during pregnancy and older age, Pb is also released from bone back into blood (2013 ISA; 2006 AQCD).

1.3.2.1 Population Blood Pb Levels By Age and Demographic Group Over Time

Over the last four and a half decades, blood Pb levels (BLLs) in the U.S. population have declined dramatically, with the most substantial reduction occurring between the 1970s and 1990s. Across ages, the age group with the highest levels is young children, aged one to five years (as discussed below). The median level for this age group declined more than a factor of four from 15 μg/dL in the late 1970s to 3.5 μg/dL by the late 1980s, and has declined by nearly another factor of six since that time, to 0.6 μg/dL in the 2017-2018 NHANES. Similar reductions have also been documented in adults older than 19 years (Table 1-2). The reductions have also been documented at the upper ends of the distribution. For example, the 95th percentile blood Pb concentration for young children has declined from 29 μg/dL in the late 1970s to 12 μg/dL in the late 1980s to 2 μg/dL in the 2017-2018 NHANES, more than a factor of 10 in all (Table 1-2; CDC, 2021). This is also illustrated by the decline in blood Pb concentrations in young children that exceeded 5 μg/dL through the 1990s, during which the prevalence of such levels dropped by 80 to 90% (Figure 1-2). This period, from the late 1970s through the 1990s corresponds to the phase out of leaded gasoline in all cars and trucks.

Table 1-2. Changes in blood Pb concentrations from the first to second NHANES.

NHANES Years	Median Concentration (μg/dL)		95th Percentile Concentration (μg/dL)	
	1-5 years	≥ 20 years	1-5 years	≥ 20 years
1976-1980	15	13	29	26
1988-1991	3.5	3.2	12	9.5
Sources: Pirkle et al., (1994) and U.S. EPA., (2013b).				

The 1976-1980 NHANES blood Pb levels were strongly associated with usage of leaded gasoline (metric tons per day) and population blood Pb levels (Schwartz and Pitcher, 1989). Although national estimates of blood Pb concentrations are not available prior to the 1976-1980 NHANES, the relationship of blood Pb concentrations with leaded gasoline usage indicates the blood Pb concentrations at that time may be a reasonable representation of levels during previous years of leaded gasoline usage. Leaded gasoline was used in U.S. on-road vehicles from the 1930s through 1990s, with usage peaking in the 1970s (2013 ISA, Figure 2-7). Estimated U.S. air Pb emissions in 1970 was more than 200,000 tons, with a subsequent declining trend dominated by highway vehicle emissions through 1985, by which time the national estimate from all sources had dropped by more than an order of magnitude from 1970 (2013 ISA, Figure 2-1).

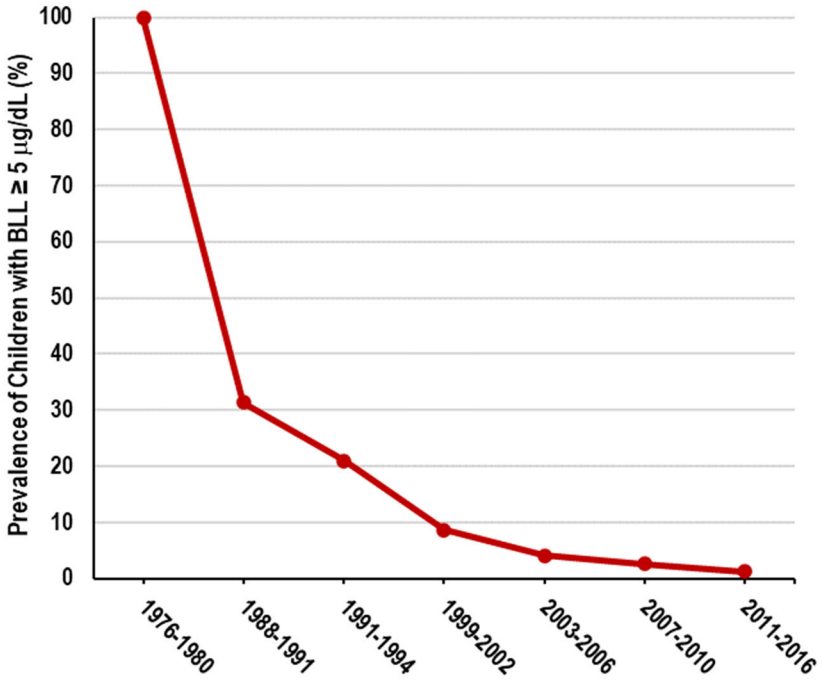


Figure 1-2. Prevalence of blood Pb concentrations at or above 5 µg/dL in children, aged 1-5 years (from Egan et al. [2021] Table 4).

As individuals age, behaviors that influence exposure, such as crawling and hand-to-mouth contact of babies and toddlers, change, such that exposures via some significant pathways are reduced. This contributes to the lower blood Pb levels observed in primary school children compared to pre-school age children, one to five years old (Figure 1-3).[3] Factors that contribute to adult blood Pb levels being higher than teenage blood Pb levels include higher exposures of individuals in that age group during their earlier years (compared to those of the teenagers), bone remodeling in older adults in the age group, and, potentially, contributions from occupational exposures (Figure 1-3; 2013 ISA, 2006 AQCD; draft ISA, Appendix 2). As can be seen from Figure 1-3, blood Pb levels (BLLs) have continued to decline in all ages (Figure 1-3).

[3] Since 1976, the U.S. Centers for Disease Control and Prevention (CDC) has been monitoring blood Pb levels nationally through the National Health and Nutrition Examination Survey (NHANES) and provides nationally representative biomonitoring data for Pb. NHANES is designed to assess the health and nutritional status of the civilian noninstitutionalized U.S. population and is conducted by the National Center for Health Statistics, part of the CDC. The NHANES involves interviews and physical examinations with approximately 10,000 people in each two-year year survey cycle. CDC's National Center for Environmental Health measures concentrations of environmental chemicals in blood and urine samples collected from NHANES participants. Summaries of the measured values for lead and more than 200 other chemicals since 1999-2000 are provided in the CDC's National Report on Human Exposure to Environmental Chemicals (CDC, 2022).

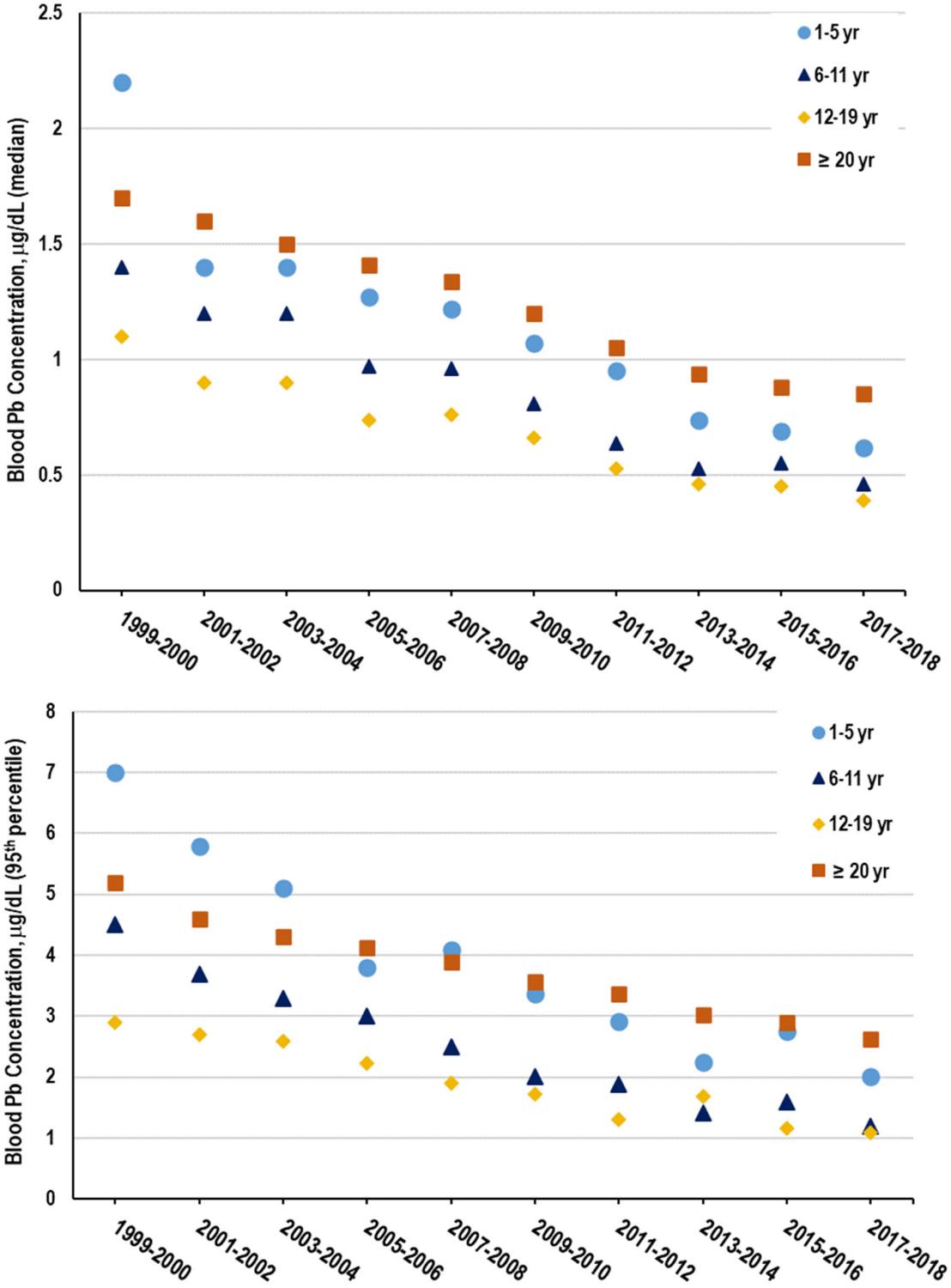


Figure 1-3. Blood Pb concentration estimates in the general population by age group from NHANES (CDC, 2021) for median (upper panel) and 95th percentile (lower panel).

Although blood Pb levels in U.S. children have declined, the mean blood Pb levels reported in NHANES consistently differ among children of different ethnic backgrounds, and for children from low-income households compared to the general population as a whole. More specifically, blood Pb levels for non-Hispanic Black children have historically been higher than levels for White children and for other minority populations, as well as for the U.S. population of children as a whole (Figure 1-4; 2013 ISA, sections 3.4.1, 5.2.1.1 and 5.2.3). Similarly, blood Pb levels in children from low-income households have also been historically higher than those for other households. For example, among children, ages one to five years, in the1991-94 NHANES, the median blood Pb level for non-Hispanic Black children was nearly two-fold higher than the median for White non-Hispanic children (4.3 μg/dL compared to 2.3 μg/dL), as seen in Figure 1-4. Additionally, the median blood Pb level in young children from low-income households in 1991-94 NHANES was nearly 1.5 times higher than the median for the general population as a whole (4.1 μg/dL compared to 2.6 μg/dL) (U.S. EPA 2022).

The reductions in blood Pb levels across the last several decades have occurred across these demographic groups. Further, the gap between blood Pb levels from these populations compared to the general population has also narrowed (Figure 1-4). For example, while the 1991-94 median Pb lead level in non-Hispanic Black children was nearly 2-fold higher than the median for White children, by the 2013-2016 NHANES, the median blood Pb level for non-Hispanic Black children had decreased to 0.9 μg/dl, less than 30% higher than the median of 0.7 μg/dl for White children (Figure 1-4; U.S. EPA 2003, 2013b, 2019, 2022c). Similarly for low-income children, the difference in median blood Pb level from that for the full population narrowed from nearly a factor of 1.5 in 1991-94 to less than 30% (e.g., 0.9 μg/dL compared to 0.7 μg/dL) by the 2013-16 NHANES (U.S. EPA, 2022).

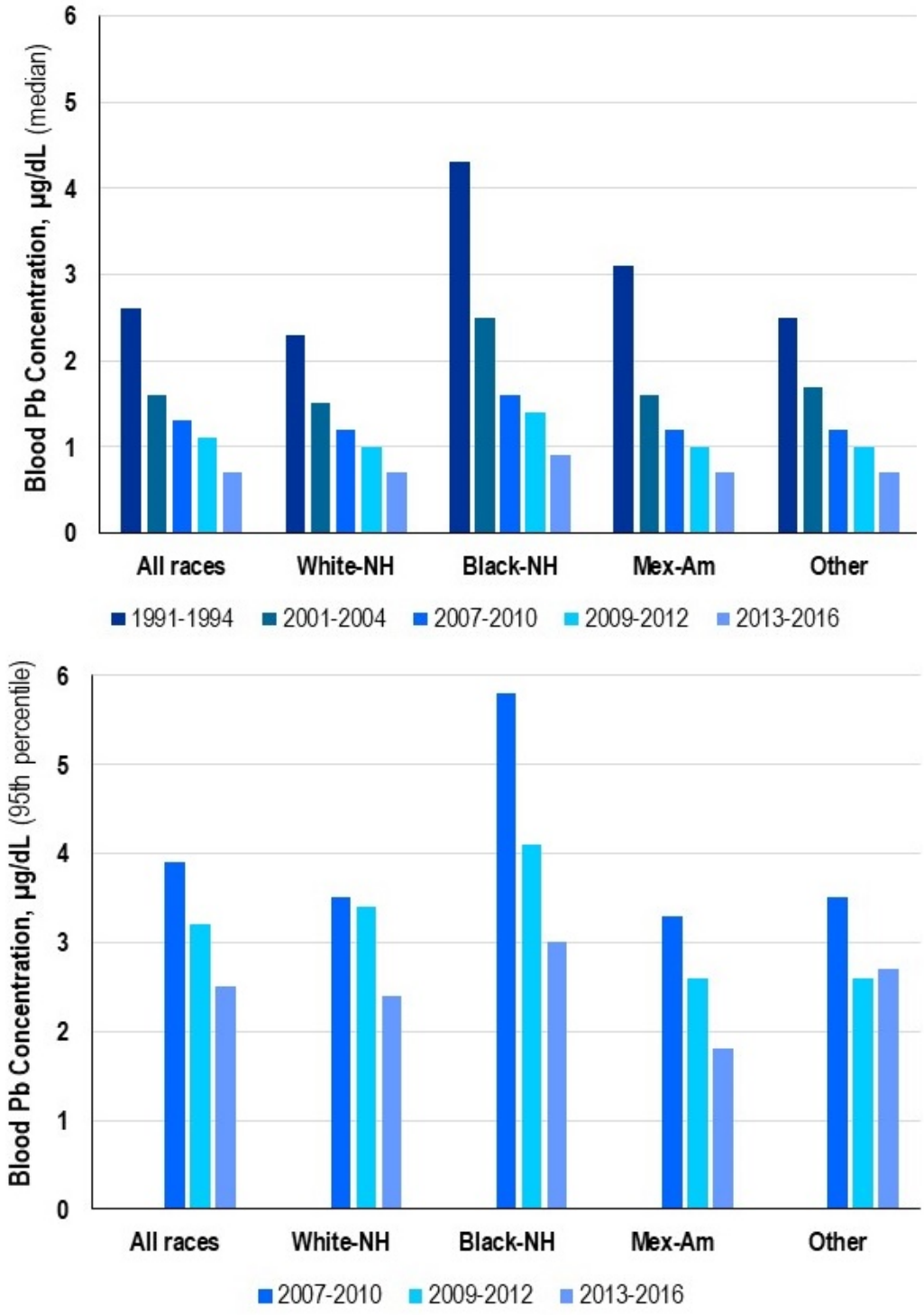


Figure 1-4. Median (upper panel) and 95th percentile (lower panel) blood Pb estimates from NHANES for young children, aged one to five years, of differing race. NH, non-Hispanic; Mex-Am, Mexican American.

1.3.2.2 Cumulative Exposure for Different Birth Cohorts

Cumulative Pb exposure may be indicated by bone Pb concentration (e.g., tibia) or a cumulative blood Pb metric derived from longitudinal BLL (2013 ISA, section 3.3.1). Blood Pb is an indicator of Pb that is circulating through an individual at a point in time and, accordingly, may best reflect recent exposures and to some extent past exposure depending on factors like age and disease state, as well as differences of past and recent exposures. It cannot, however, fully reflect an individual's exposure history. Because Pb is stored in the bone, bone Pb is considered to provide a measure of an individual's cumulative lifetime exposure. Additionally, where longitudinal blood Pb measurements are available, a cumulative blood Pb metric is also informative regarding an individual's exposure across their lifetime. A cumulative blood Pb metric may be derived in a manner conceptually similar to a cumulative exposure metric often employed in worker studies (e.g., using ppm-days). The metric is derived essentially by multiplying blood Pb measurement by years to which it is applied yielding an index in terms of (μg/dL)·years (e.g., Nie et al., 2011 and Somervaille et al., 1988; 2013 ISA, section 3.3.1).

Given the backdrop of dramatic reductions in Pb exposures over the past four plus decades, as evidenced in blood Pb levels of young children during that time, adults in the U.S. population have significant Pb exposure histories. Further, adults of different ages may have appreciably different exposure histories. This is especially true of adults who lived through periods of the use of leaded on-road motor vehicle fuel compared to much younger adults. Such differences in exposure history can be illustrated through use of a cumulative blood Pb index (CBLI), a metric sometimes used as an exposure metric in epidemiological studies of adult populations (2013 ISA, section 3.3.5; Nie et al., 2011; Hu et al., 2007; Somervaille et al., 1988).

Estimates of CBLI[4] for different birth cohorts, the derivation of which is described in more detail in the Appendix, can illustrate of the appreciably different Pb exposure histories of adults in today's population and the difference of those histories from adults of tomorrow (Table 1-3). The limitations in the analysis, and its underlying datasets, and associated uncertainties associated with the resultant CBLI estimates (as summarized in the Appendix) are important considerations in their interpretation. Consistent with these considerations, the estimates in Table 1-3 provide a sense of the magnitude of the differences in exposure histories for several birth cohorts of the U.S. general population that are represented among the adults of today and the future.

[4] The CBLI is calculated as: $CBLI = \sum_{i=1}^{n} 0.5 \times (PbB_{i+1} + PbB_i) \times (t_{i+1} - t_i)$, where blood Pb_i and blood Pb_{i+1} are the blood lead concentrations at two consecutive times t_i and t_{i+1}.

Table 1-3. Age-specific cumulative lead exposures estimated for general population cohorts born in the years 1945, 1970, 1990 and 2010.

Age (years)	CBLI Estimate, (μg/dL)·yrs, at Specified Age for Cohorts Born in:			
	1945	1970	1990	2010
5	74 [A]	74 [A]	89	4.3
10	139 [A]	139 [A]	23	7 [B]
21	274 [A]	197	33 [C]	12 [B]
30	395	212	39 [C]	16 [B]
50	549	235 [D]	53 [C]	24 [B]
75	587	256 [D]		

[A] Estimated CBLI for ages ≤25 for the 1945 cohort and ≤10 for the 1970 cohort occur in years before the earliest NHANES (1970), which may contribute a bias low given higher Pb exposures from the use of leaded gasoline. See Appendix for details.

[B] Estimated CBLI for ages at/above 10 years for the 2010 cohort are projected. In CBLI derivation, the most recent NHANES estimates (2018) were used, which may contribute a bias high given backdrop of declining Pb exposures. See Appendix for details.

[C] Estimated CBLI for ages at/above 20 years for the 1990 cohort are projected. In CBLI derivation, the most recent NHANES estimates (2018) were used, which may contribute a bias high given backdrop of declining Pb exposures. See Appendix for details.

[D] Estimated CBLI for ages at/above 48 years for the 1970 cohort are projected. In CBLI derivation, the most recent NHANES estimates (2018) were used, which may contribute a bias high given backdrop of declining Pb exposures. See Appendix for details.

As illustrated described in section 1.3.2.1 above, NHANES blood Pb estimates for low-income and non-Hispanic Black populations have historically been appreciably greater than those for the general population. The ramifications of this on estimates of cumulative childhood exposure for cohorts born in 1990 and 2010 is illustrated by CBLI estimates presented in 0. Notably for the 2010 birth cohort, while the CBLI estimate for the non-Hispanic Black population is still slightly greater than that for the full cohort (all races), the gap between the two is considerably narrower relative to its size for the 1990 birth cohort.[5]

[5] Based on NHANES estimates and trends for low-income children, a similar pattern would be expected for low-income cohorts.

Table 1-4. Age-specific cumulative lead exposures estimated for non-Hispanic Black and full population child cohorts born in the years 1990 and 2010.

	CBLI Estimate, (μg/dL)·yrs, at Specified Age* for Cohorts Born in:			
	---------- 1990 ----------		---------- 2010 ----------	
Age (years)	Full Population	Non-Hispanic Black	Full Population	Non-Hispanic Black
5	14	21	4.3	5.4
10	23	35	7.0	9.6

* CBLI for ages older than 10 has not been estimated in this table as NHANES blood Pb estimates are not readily available for the 11-19 year old age range for non-Hispanic Black demographic group, although they are for the full population. Accordingly, estimates for ages older than 10 would not be of comparable basis.

2 QUANTITATIVE ANALYSIS PLANNING FOR THE PRIMARY STANDARD

In reviews of primary NAAQS, quantitative risk and exposure assessments (REAs)[6] are generally designed to assess human exposure and health risk for air quality conditions associated with the existing standards and, as appropriate, for conditions associated with potential alternative standards. The objective for such assessments is to provide quantitative estimates of impacts that inform judgments on the public health significance of exposures likely to occur under air quality conditions reflective of the current NAAQS and, as appropriate, any alternative standards under consideration. Risk estimates are also used in support of other quantitative analyses of the evidence. For example, in the 2008 Pb NAAQS review, quantitative risk estimates for specific case studies were employed in evaluation of the evidence-based framework developed to inform the Administrator's judgments on a level for the revised standard.[7] Accordingly, the assessments are also intended to provide a basis for judgments as to the extent of public health protection afforded by such standards.

In reviews of primary NAAQS, quantitative exposure and health risk assessments are generally intended to inform consideration of key policy relevant questions (see section 3.1), such as the following:

- What are the nature and magnitude of exposures and health risks associated with air quality conditions just meeting the current standard and, as appropriate, alternate air quality conditions?
- To what extent are the estimates of exposures and risks to at-risk populations associated with air quality conditions just meeting the current standard and, as appropriate, alternate air quality conditions reasonably judged important from a public health perspective?

In considering exposure and risk estimates and their interpretation in this context, an accompanying consideration is:

- What are the important limitations and associated uncertainties associated with the risk/exposure estimates?

[6] While the term REA has in the past several NAAQS reviews referred to assessments presented in a stand-alone REA document, in this review, we are also using this term, or the phrase "REA analyses" to simply refer to the analyses which we intend to present in appendices or as supplemental materials to the PA.

[7] In the 2008 review, an evidence based framework focused on air-related, Pb-attributable IQ decrements was developed that related relationships of ambient air Pb with children's blood Pb and of children's blood Pb with IQ decrements. General consistencies found between estimates derived from this evidence-based framework and risk estimates generated using the case-study based approach informed the Administrator's judgments, providing general support for the Administrator's decisions on revisions for the new standard (IRP, v1, section 3.3; 73 FR 67006, November 12, 2008).

In developing REAs in a NAAQS review, we draw upon the currently available health effects evidence that is characterized in the ISA. This includes information on atmospheric chemistry, air quality, human and environmental exposures, dosimetry and mode of action, and information on health effects associated with exposures considered likely to occur because of pollutant concentrations in ambient air. We additionally employ current methods and tools to support the quantitative modeling and assessment.

The REAs commonly rely on a case study approach, which involves quantitative analyses focused on populations and pollutant concentrations in one or more specific exposure situations reflecting air quality conditions that just meet the existing standards (and alternatives as appropriate), often through simulations for different geographic areas.[8] Reliance on this approach is intended to provide assessments of the air quality scenario(s) of interest for a set of case studies and associated exposed at-risk populations and ecosystems that will be informative to the EPA's consideration of potential exposures and risks that may be associated with the stated air quality conditions. For example, we are interested in the exposure and risk associated with air quality conditions that just meet the current standard(s); such information is useful in interpreting the degree of protectiveness given by the current standard(s), the adequacy of such standard(s), and the need to consider alternatives.

Further, the REA analyses employ a case study approach that addresses practical considerations, such as employing a tractable scale and considering resource constraints, while providing estimates for populations and/or geographic areas of interest and also having broader applicability (e.g., offering risk perspective for similar study areas that were not assessed). Thus, REA analyses are not generally intended to provide a comprehensive national assessment of such conditions, nor are they necessarily intended to provide such an assessment of existing air quality. Rather, the purpose is to assess population exposure and risk for particular air quality conditions based on currently available scientific information, modeling tools, and other technical information. As a result, the REA can provide extended perspective on potential exposures and risks in geographic areas across the U.S. not analyzed, but with similarity in the attributes that primarily influence exposures and risks, such as ambient air concentrations, population demographics, and the degree of correlation in their spatial distributions.

In planning any REA analyses that may be appropriate for a new NAAQS review, we first consider the analyses conducted in the last review and the extent to which they provided

[8] Although case studies often focus only on specific geographic locations (e.g., populations in specific urban areas), in past Pb NAAQS reviews, we have also included a generic case study intended to estimate exposure and risk for a generalized group of residential children, not linked to a specific geographic location. Rather it is characterized by exposure associated with residence near a significant source of Pb emissions such that air quality conditions just meet the standard (see section 2.1, below, for additional detail; 81 FR 71923-71924, October 18, 2016).

important insights that were informative to the Agency's decision on the current standard. Conclusions in this regard are generally influenced by an assessment of the uncertainties associated with each type of analysis and the corresponding consideration of each type's relative strength, as documented in the notice of the decision for the prior review and associated assessment documents such as the PA and REA. In considering whether new analyses are warranted for particular types of assessments, we evaluate the availability of new scientific evidence and technical information in this review, as well as improved methods and tools, that may provide support for conducting updates to address key limitations or uncertainties in analyses from the last review or to provide additional insight beyond those provided by the prior REA. Thus, we focus on identifying the new analyses that are warranted in consideration of factors such as those raised here, while also bearing in mind practical and logistical considerations such as available resources and timeline for the review.

The types of analyses performed in NAAQS reviews generally reflect the nature and strength of the evidence in various aspects. For example, for the health effects pertaining to exposures associated with the presence of the pollutant in ambient air, the availability and type of information from the health effects literature on relationships between internal dose, exposure, or ambient air concentration and health response influences the types of exposure assessment and risk characterization that are performed. The health risk assessments focus on exposure metrics that are appropriate for effects of concern for the subject pollutant and, along with available ambient air concentration measurements and model estimates, where appropriate, are used to generate estimates of exposure. Consistent with the health risk approaches that have been used in NAAQS reviews (illustrated in Figure 2-1), assessments of air-related health risks of Pb in past reviews have been based on estimating internal concentrations of the biomarker, blood Pb, and then employing a concentration-response (C-R) function-based approach to estimate risk.

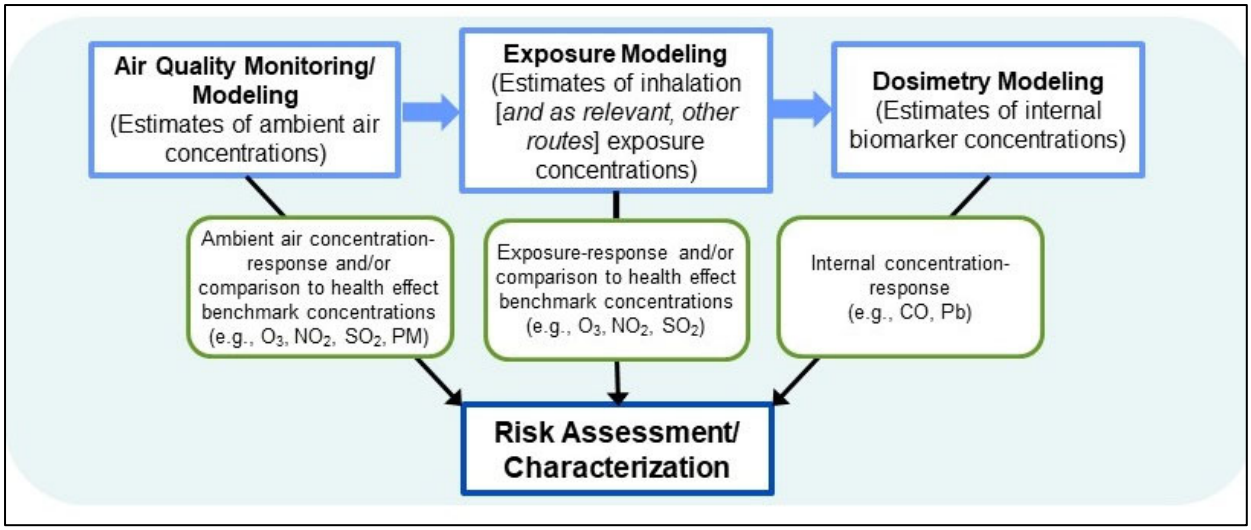


Figure 2-1. Summary of health risk assessment approaches that have been employed in NAAQS reviews.

The purpose of the sections below is to briefly summarize the comprehensive, complex, and resource-intensive quantitative health and welfare risk assessments completed in past reviews of the Pb NAAQS, giving attention to those analyses concluded to be most informative to the decisions reached on the standards. In considering the issues raised above, we additionally summarize key uncertainties and limitations of the analyses conducted for the last review and consider the extent to which newly available information, tools or methodologies might address those areas. For example, the scope of any analyses for this review would be informed by the new scientific information characterized in the upcoming ISA; recent air quality data; the availability of improved data, methods, tools, and models that can be used to address limitations and uncertainties from the last review; and any constraints on resources and the review timeline. Consideration is also given to a review of the way risk information has been used to address specific science-policy questions in previous NAAQS reviews and whether that application identifies specific areas of uncertainty or limitations that could be addressed to enhance the utility of the risk assessment in informing NAAQS reviews going forward.

We are planning that the quantitative exposure and risk analyses newly developed in this review will be described in the PA, and we plan to consider these analyses along with any previously conducted analyses that remain pertinent and informative to consideration of the adequacy of the current standard (and alternative standards, as appropriate). We intend to provide associated technical details for any new exposure and risk analyses in appendices or supplemental materials for the PA, while analyses from the prior reviews are described in the documents for those reviews. Any quantitative assessments newly developed in this review would then be made available for public comment and reviewed by the CASAC in the context of

the draft PA. Public comments and CASAC advice on such REA-related analyses in the draft PA would be considered in finalizing analyses for presentation in the final PA.

In this chapter, we summarize the types of analyses performed in the last review and highlight some considerations for analyses in this review. The exposure and risk analyses performed in past Pb NAAQS reviews are described in section 2.1 below, along with a summary of key uncertainties and limitations. The roles of the risk analyses in informing both the 2008 and 2016 NAAQS reviews are also summarized in section 2.1 with a focus on identifying key uncertainties and limitations that informed interpretation of that risk information. In section 2.2, we discuss key considerations relative to the refinement and updating of the 2007 REA for use in the current review with emphasis on the availability of new information that can address key limitations and uncertainties identified in section 2.1. Based on the information presented in sections 2.1 and 2.2, we then present our preliminary plans for developing an REA to support the current review in section 2.3.

2.1 ASSESSMENTS INFORMING THE LAST REVIEW

The exposure and risk information available for consideration in the 2016 review was drawn primarily from the 2007 REA (80 FR 300–305, January 5, 2015).[9] The 2007 risk assessment focused on assessment of Pb-attributable IQ decrements in young children residing in areas with air quality just meeting a set of potential alternative primary standards. The assessment, with its focus on Pb derived from sources emitting Pb to ambient air, employed several different case studies, as described below. As the air quality scenarios included in the 2007 assessment had not included the existing primary standard, the 2007 information was enhanced for the 2016 review by the inclusion of a limited new computation for one case study focused on risk associated with the existing standard (2014 PA, section 3.4 and Appendix 3A). Key aspects of the exposure and risk assessment considered in the 2016 review are described below.

The conceptual model that informed planning for the 2007 REA identified sources, pathways, routes, exposed populations, and health endpoints. The multimedia and persistent nature of Pb, as well as the existence of many non-air sources of Pb to the environment, contributed multiple complexities to the exposure and risk assessment for ambient air related Pb.

[9] The information newly available in the 2016 review, with regard to designing and implementing a full REA for that review, was such that performance of a new REA for that review was not warranted, a decision with which the CASAC Pb Review Panel generally concurred. In that review, after careful consideration of the available information regarding designing and implementing a full REA, the EPA determined that the available information did not provide the means by which to develop an updated or enhanced risk model that would substantially improve the utility of risk estimates in informing the current Pb NAAQS review (2011 REA Planning Document, section 2.3).

Sources of human Pb exposure include current and historical air emissions sources, as well as miscellaneous non-air sources, which can contribute to multiple exposure media and associated pathways (e.g., inhalation of ambient air, ingestion of indoor dust, outdoor soil/dust and diet or drinking water). As illustrated in Figure 2-2 below, in addition to airborne emissions (recent or those in the past), sources of Pb to these pathways also include old leaded paint, and associated Pb mobilized indoors during renovation/repair activities, and in soils. Further, Pb in diet and drinking water may have air pathway-related contributions as well as contributions from non-air sources (e.g., Pb solder on water distribution pipes and Pb in materials used in food processing).

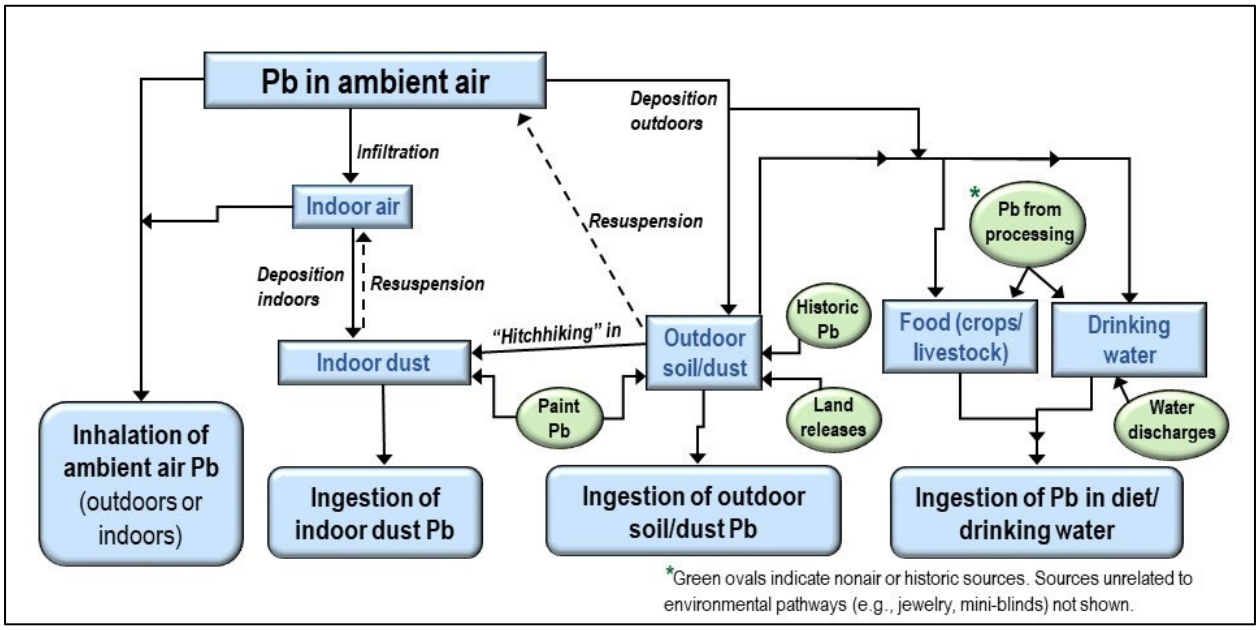


Figure 2-2. Simplified presentation of air-related Pb exposure pathways.

Although our focus for the assessment was on the ambient-air aspects of Pb exposure that are most relevant to the standard, limitations in the available data and modeling tools affected characterization of the various complexities of ambient air Pb pathways and handicapped our ability to separate the non-air contributions to Pb exposure from estimates of air related Pb exposure and risk. As a result, the assessment included several simplifying assumptions in a number of areas, which produced estimates of air-related Pb risk that are approximate and are characterized by upper and lower bounds. The lower bound is based on a combination of pathway-specific estimates that do not completely represent all air-related pathways, while the upper bound is based on a combination of pathway-specific estimates that includes pathways that are not air-related but the separating out of which is precluded by modeling and data limitations (81 FR 71925, October 18, 2016).

To inform our understanding of air-related exposure and risk in different types of air Pb exposure situations, Pb exposure and associated risk were estimated in the 2008 review for

multiple case studies that generally represent two categories of residential population exposures to air-related Pb: (1) location-specific urban populations of children with a broad range of air-related exposures, reflecting existence of concentration gradients, and (2) children residing in localized areas with air-related exposures representing air concentrations specifically reflecting the standard level being evaluated (see Table 2-1). Accordingly, the two categories of case studies differed with regard to the extent to which they represented population variability in air-related Pb exposure. The case studies developed included two point source-focused case studies. One was a small rural community near a secondary Pb smelter (not shown in Table 2-1[10]), and the second was a community near a primary Pb smelter. For the latter, two different sets of estimates were derived, one for the nearest residents for whom dust-related exposures were most significant and a second set of estimates for somewhat more distant residents (e.g., falling into the first of the two categories), using tools and data particular to each community's exposure circumstances (2007 REA, section 2.2). Also in the first category were three location-specific urban case studies in the metropolitan areas of Cleveland, Chicago and Los Angeles.

Table 2-1. Summary of approaches used to estimate case study media concentrations in 2007 REA (based on 2014 PA, Table 3-7).

Type of Population Exposure			Case Study
Broad range of air-related exposures	Part of metropolitan area with spatially varying air concentrations, inclusive of location at standard or conditions being evaluated	Multiple exposure zones, larger populations	**Location-specific urban:** Cleveland, Chicago, Los Angeles
	As above, with dominant, historically active metals industry as ambient air Pb source		**Primary Pb smelter (full study area)**
Generalized, high end of air-related exposure	Localized residential area with air concentrations generally representing the standard or conditions evaluated	Single exposure zone without enumerated population	***Generalized local***
		A few exposure zones with small population	**Primary Pb smelter (subarea)**

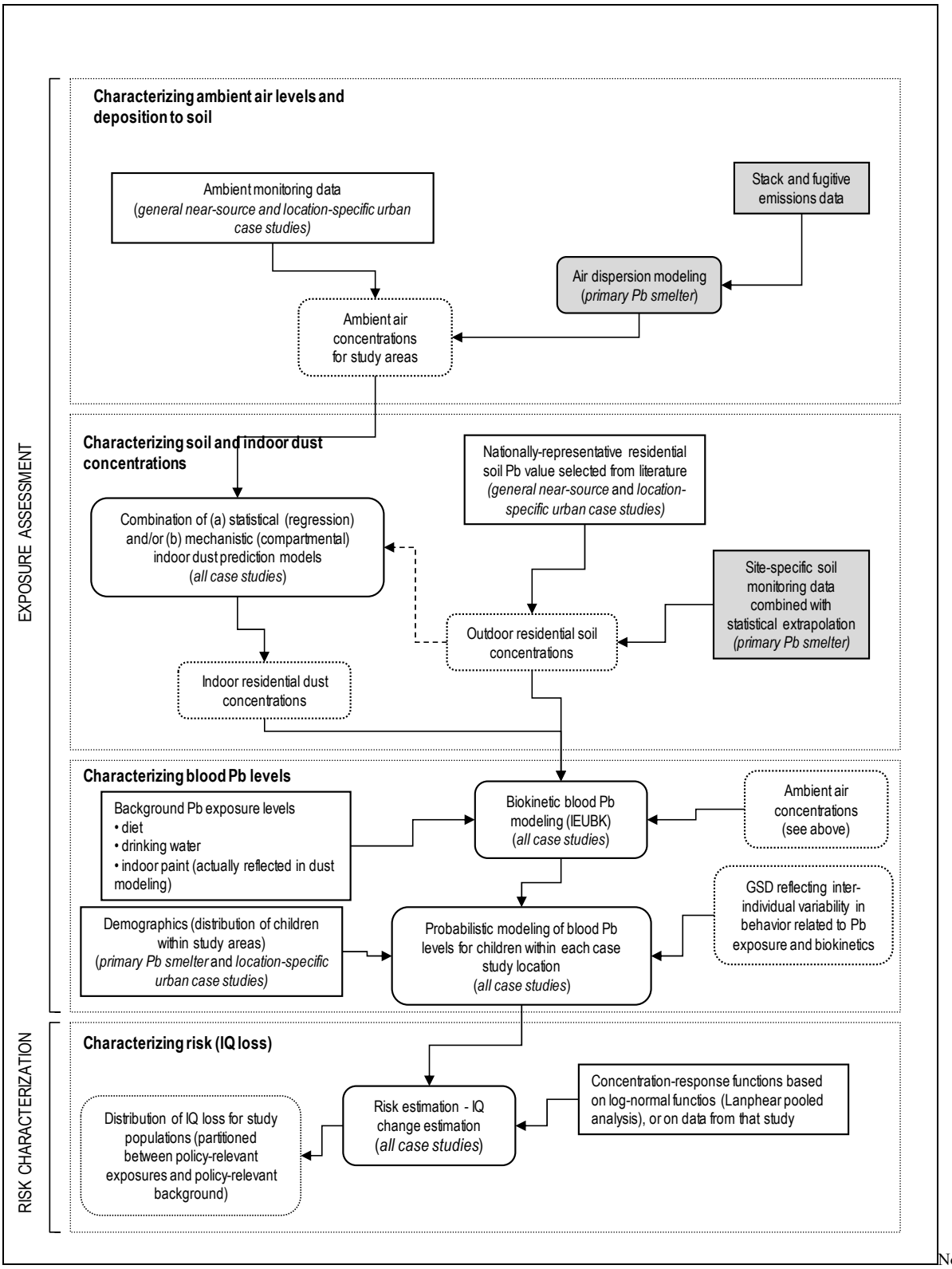
Two case studies, one from each of these two categories, were considered to be most useful in the 2016 review: (1) the location-specific urban case study for Chicago and (2) the generalized local case study. The generalized local case study (referred to as general urban case study in the 2008 and 2016 reviews) was not based on a specific geographic location and

[10] Due to uncertainties associated with modeling ambient air impacts of Pb emitted from the secondary Pb smelter and potential to underestimate exposure and risk impacts to residential populations within the study area (see 2007 REA, section 4.3.1), this case study did not weigh heavily in past reviews.

reflected several simplifying assumptions in representing exposure, including uniform ambient air Pb levels associated with the standard of interest across the hypothetical study area and a uniform study population. Based on the nature of the population exposures represented by the two categories of case study (see Table 2-1), the generalized local case study includes populations that are relatively more highly exposed by way of air pathways to air Pb concentrations near the standard level evaluated, compared with the populations in the location-specific urban case. The location-specific urban case studies provided representations of urban populations with a broad range of air-related exposures due to spatial gradients in both ambient air Pb levels and population density. For example, the highest air concentrations in these case studies (i.e., those closest to the standard being assessed) were found in very small parts of the study areas, while a large majority of the case study populations resided in areas with much lower ambient air concentrations.

2.1.1 Summary of Design Aspects of the 2007 Assessment

The approach to assessing exposure and risk for the two categories of case studies identified above (urban location-specific and generalized local) was comprised of four main analytical steps (Figure 2-3): (1) Estimation of ambient air Pb concentrations, (2) estimation of Pb concentrations in other key exposure media, including outdoor soil and indoor dust, (3) use of exposure media Pb concentrations, with other pathway Pb intake rates (e.g., diet), to estimate blood Pb in children using biokinetic modeling, and (4) use of C–R functions derived from epidemiological studies to estimate IQ decrements associated with the blood Pb. Concentrations of Pb were estimated in media and indoor dust using a combination of empirical data and modeling projections. The use of empirical data brings with it uncertainty related to the potential inclusion of non-air source signals in these measurements (e.g., house paint contributions to indoor dust and outdoor soil Pb). Conversely, the use of modeling tools introduces other uncertainties (e.g., model and parameter uncertainties).



Note, the greyed-out boxes reference study areas that ultimately did not receive as much focus in the 2016 NAAQS review.

Figure 2-3. Analytical approach for two case study categories in 2016 review.

Characterization of Pb in ambient air relied on (1) the use of ambient air monitor data for the location-specific urban case studies and (2) an assumption of uniform ambient air Pb levels (just meeting the standard being considered) for the generalized local case study. The ambient air monitors within each location-specific urban case study were used to characterize spatial gradients. By contrast, the generalized local case study is designed to assess exposure and risk for a smaller group of residents (e.g., neighborhood) exposed at the standard, and, therefore, ambient air Pb concentration was fixed at the standard being assessed. For the generalized local case study, which has a single exposure zone in which air Pb concentrations do not vary spatially, we derived a single air Pb concentration estimate to meet the standard assessed. Concentrations in the location-specific urban study areas, which relied on empirical (monitor-based) data to define ambient air Pb concentrations, reflected contributions from all sources affecting the concentrations in those locations, potentially including currently active stationary or mobile sources, resuspension of previously deposited Pb or other sources.

The air quality scenarios assessed in the 2008 review included air quality associated with a set of potential alternative standards more restrictive than the then-existing standard under review (1.5 $\mu g/m^3$ as a not to be exceeded calendar quarter average): a maximum calendar quarter average of 0.2 $\mu g/m^3$ and maximum monthly averages of 0.5, 0.2, 0.05 and 0.02 $\mu g/m^3$ (2014 PA, Table 3–8). However, in estimating concentrations of Pb in media that might be affected by reductions in the standard, the full multimedia impact was not simulated due to limitations in the available data and modeling tools that precluded simulation of linkages between some media and air Pb. Specifically, as shown in Table 2-2 below, while Pb concentrations in indoor dust were simulated to differ among the different air quality scenarios for which there were differing ambient air Pb concentrations (outdoors and indoors), dietary and drinking water Pb concentrations, as well as soil Pb concentrations, were not varied across the air quality scenarios in any case study (2014 PA, Table 3–7).

Table 2-2. Summary of approaches used to estimate case study media concentrations in 2007 REA (based on 2014 PA, Table 3-7).

Simulation of air quality impacts	Media category	Generalized local case study	Location-specific urban case study
Concentrations for these media **were varied** across air quality scenarios (see 2014 PA, section 3.4.3.2).	**Ambient air Pb**	Constant ambient air Pb just meeting standard across entire study area (single exposure zone)	Source and non-source monitors define concentration gradient (6 to 11 exposure zones per case study)
	Indoor dust Pb	a) Hybrid model with a dynamic aspect relating ambient air Pb concentrations to indoor dust Pb, and empirical aspect representing other contributions (e.g., paint, historical air, Pb carried indoors with people) (2007 REA, section 3.1.4) b) Ambient air-only regression model from literature (2007 REA, section 3.1.4)	
Concentrations **were constant** across air quality scenarios (data/modeling limitations)	**Outdoor soil Pb**	National dataset (HUD, for houses constructed between 1940 and 1998; 2007 REA, section 3.1.3).	
	Dietary Pb	National datasets for Pb residue data (US FDA Total Diet Study) and food consumption data (NHANES) (2007 REA, Appendix H, Table H-6)	
	Drinking water Pb	US and Canada datasets for residential water Pb concentrations and ingestion rates (2007 REA, Appendix H, Table H-6)	

In estimating blood Pb using the Integrated Exposure and Uptake Biokinetic (IEUBK) model,[11] Pb concentrations in exposure media (e.g., ambient air, diet, water, indoor dust) were held constant throughout the 7-year simulation period, while behavioral and physiological variables were changed with age of child (2007 REA, sections 3.2.1.1 and 5.2.4).[12] For all case studies, population variability in Pb intake and uptake was simulated by Monte Carlo-based population sampling around a mean blood Pb from IEUBK modeling and a geometric standard deviation (GSD) representing children's blood Pb variability (2014 PA, section 3.4; 2007 REA, Appendix H).[13] The risk characterization step generated a distribution of IQ decrement estimates for the set of children simulated in the assessment.

Specifically, blood Pb estimates for the concurrent blood Pb metric were combined with four C–R functions for IQ decrements derived from the analysis by Lanphear et al. (2005) of a

[11]The IEUBK model simulates exposure of children to Pb from multiple sources and through various routes including inhalation and ingestion. Model inputs include soil-Pb concentration, air-Pb concentration, dietary-Pb intake including drinking water, Pb-dust ingestion, human activity, and biokinetic factors (2013 ISA, p. 1-11).

[12] Detail on methods used to characterize media Pb concentrations and all IEUBK inputs for each case study are in the 2007 REA, sections 3.1, 3.2, 5.2.3 and 5.2.4, and Appendices C through H.

[13] This GSD reflects a number of factors which operate together to produce interindividual variability in blood Pb levels, including: (a) biokinetic variability (differences in the uptake, distribution or clearance of Pb), (b) differences in behavior related to Pb exposure (e.g., varying hand-to-mouth activity, tap water ingestion rates, and time spent playing indoors) and (c) differences in environmental Pb exposure concentrations (e.g., spatial gradients in ambient Pb levels of a resolution beyond that simulated in each case study, differences in cleaning/vacuuming rates and air exchange rates) (see 2007 REA, section 3.2.3).

pooled international dataset of blood Pb and IQ (see the 2007 REA, section 5.3.1.1).[14] We used the four different C–R functions to provide different characterizations of the blood Pb-IQ decrements relationship at low exposures in recognition of uncertainty related to modeling this endpoint, particularly at lower Pb levels for which there is limited or no representation in the Lanphear et al. (2005) pooled dataset. Consideration of the risk estimates focused on estimates for one of the four functions (referred to as the loglinear with low-exposure linearization C–R function [2014 PA, section 3.4.3.3; 2007 REA, section 4.2.1]).[15] The range of risk estimates reflecting all four C–R functions provides perspective on the impact of uncertainty in this key modeling step. Among the estimates based on the loglinear function, the focus in the 2016 review was on the median IQ decrement estimates (as in the 2008 review), due to increased confidence in these estimates relative to the higher percentile estimates, for which significant uncertainty is recognized (2014 PA, sections 3.4.5, 2.4.6 and 3.4.7; 2007 Staff Paper, p. 4-20).

As the 2007 REA did not include an air quality scenario simulated to just meet the standard that was established by the 2008 decision, two different approaches were employed in the 2016 review to estimate risk pertaining to conditions just meeting the standard set in 2008. First, given the similarity of the then-current condition scenario for the Chicago case study (among all the 2007 REA scenarios) to the current standard (set in 2008), the risk estimates for that scenario were considered to be informative with regard to risk associated with the current standard. To augment the risk information available in the 2016 review and in recognition of the variation among specific locations and urban areas with regard to air quality patterns and exposed population, estimates for an air quality scenario just meeting the current Pb NAAQS were newly developed in the 2016 review in the context of the generalized local case study. These estimates were derived based on interpolation from the risk estimates available for scenarios previously assessed for the generalized local case study. Such interpolated estimates were only developed for the generalized local case study due to its use of a single exposure zone which greatly simplified the method employed.[16]

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[14] The four C-R functions each involved different approaches to estimating IQ decrement at and below the lowest blood Pb measurements analyzed in Lanphear et al.(2005). Entry K in Table 2-3 provides more detail.

[15] Of the four functions, this function is nonlinear in shape, overall, reflecting the differing response at different blood Pb concentrations consistent with Lanphear et al. (2005); is based on a function fit to the entire polled dataset, and for which sensitivity analyses indicate model coefficients to be robust (Lanphear et al., 2005); and provides an approach for estimating IQ decrements at the lowest exposures simulated, which for some is below those studied (2007 REA).

[16] Interpolation of risk estimates to estimate risk for the current standard was not done for other case studies because those case studies utilized a more complex, spatially-differentiated and population-based approach. Application of the simple linear interpolation approach for those case studies would have introduced substantial additional uncertainty (relative to the other estimates for the same case study). The simplicity of the generalized local study area, however, with its single exposure zone, is amenable to the linear interpolation of risk described here.

In the 2016 review, the approach employed to develop estimates for the existing standard (established in 2008) in the generalized local case study was to identify two potential alternative standard scenarios that had been simulated in the 2007 REA for air quality conditions bracketing those for the existing standard and then linearly interpolate an estimate of risk for the current standard based on the slope created from the two bracketing estimates (2014 PA, section 3.4.3.3.2 and Appendix 3A). By this method, the air quality scenario for the existing standard (0.15 $\mu g/m^3$, as a not-to-be-exceeded 3-month average) was found to be bracketed by the scenarios for the potential alternative standards of 0.20 $\mu g/m^3$ (maximum calendar quarter average) and 0.20 $\mu g/m^3$ (maximum monthly average). Using interpolation between the median risk estimates for these two scenarios, median risk estimates were developed for the existing standard (2014 PA, Appendix 3A).

2.1.2 Characterization of Variability

With regard to the exposure/risk information, several important sources of variability in air-related Pb exposures and associated risk were recognized; the approaches by which they were addressed in the 2007 REA are summarized here (2014 PA, section 3.4.6; 80 FR, 303-304, January 5, 2015).

- Variation in distributions of potential residential exposure and risk across U.S. urban residential areas is addressed by the inclusion of location-specific urban study areas that reflect a diverse set of urban areas in the U.S.
- Representation of a more highly exposed subset of urban residents potentially exposed at the level of the standard is addressed by the inclusion of the generalized local study area.
- Variation in residential exposure to ambient air Pb within an urban area of the location-specific case studies is addressed through the partitioning of these study areas into exposure zones to provide some representation of spatial gradients in ambient air Pb and their interaction with population distribution and demographics.
- Inter-individual variability in blood Pb levels is addressed through the use of empirically derived GSDs to develop blood Pb distribution for the child population in each exposure zone, with GSDs selected particular to each case study population.
- Inter-individual variability in IQ response to blood Pb is addressed through the use of C–R functions for Pb-associated IQ decrement based on a pooled analysis reflecting studies of diverse populations.

2.1.3 Key Limitations and Uncertainties

In characterizing risk associated with Pb from air-related exposure pathways in the 2008 review, we faced a variety of challenges and employed a number of methods in order to develop characterizations. The challenges related to significant data and modeling limitations which affected our ability to parse out the portion of total (all-pathway) blood Pb and IQ decrement

attributable to air-related pathways, as well as our representation of key sources of variability (summarized in section 2.1.2 above) and characterization of uncertainty.

With regard to parsing out the air-related blood Pb and risk estimates, we recognized that Pb in diet and drinking water sources may in part be derived from Pb in ambient air, as well as Pb from nonair sources, but limitations precluded explicit modeling of the contribution from air-related aspects of these exposure pathways, such that the air-related component of these exposures was not estimated. Although we separated total estimates into risk estimates for diet/drinking water and two air-related categories (‘‘recent air’’ and ‘‘past air’’), significant limitations in our modeling tools and data resulted in an inability to parse risk estimates specific to the air-related pathways. Thus, we focused on estimates from the two air-related categories (“recent” and “past”), which we considered to under- and over-estimate air-related risk, respectively, to create bounds within which we consider air-related risk to fall.

The “recent” air-related category included Pb exposure pathways tied most directly to ambient air, which consequently have the potential to respond relatively more quickly to changes in air Pb (i.e., inhalation and ingestion of indoor dust Pb derived from the infiltration of ambient air Pb indoors). Importantly, media concentrations associated with the pathways in this category were simulated to change in response to air concentrations (see section 2.1.1 and Table 2-2 above; 2014 PA, section 3.4.3.1; 80 FR 300-305, January 5, 2015). The air-related Pb exposure pathways in the “past air” category, all of which are associated with atmospheric deposition, included ingestion of Pb in outdoor dust/soil and ingestion of the portion of Pb in indoor dust that after deposition from ambient air outdoors is carried indoors with humans. While there is some potential for the “past” air-related category of exposures to be affected (over some time frame) by changes in ambient air Pb concentrations (e.g., associated with an adjustment to the Pb standard), limitations in our data and tools precluded simulation of that relationship. Consequently, risk estimated for this category reflects media measurements available for the 2007 REA and is identical for all air quality scenarios. Further, although paint is not an air-related source of Pb exposure, it may be reflected somewhat in estimates developed for the “past air” category, due to modeling (and data) constraints (2007 Staff Paper, section 4.2.4). Thus, as exposures included in the “recent” air-related category do not completely capture all air-related pathways, we consider risk for this category to be an underestimate of air-related risk. Yet, as exposures included in the “past” air-related category include pathways that are not air-related, we consider the summed risk across both categories to include an overestimate of air-related risk.

In summary, because of limitations in the assessment design, data, and modeling tools, the estimates of risk attributable to air-related exposure pathways are considered to be approximate and to be bounded on the low end by the risk estimated for the “recent air” category and on the upper end by the risk estimated for the “recent air” plus “past air” categories. With

regard to the latter, modeling and data limitations reduce the extent to which the upper end of these bounds reflects impacts of the alternative air quality conditions simulated. This limitation will tend to contribute to estimates for the "past air" category representing relatively greater overestimates for relatively lower air Pb air quality scenarios (80 FR 303, January 5, 2015). In considering these risk estimates in the 2016 review, the EPA concluded that the "resultant, approximate, air-related risk bounds, however, encompass estimates drawn from the air-related IQ loss evidence-based framework, providing a rough consistency and general support, as was the case in the last review (73 FR 67004, November 12, 2008)" (81 FR 71925, October 18, 2016). The Administrator's decision in 2016, that it was appropriate to retain the existing standard, was based on consideration of the evidence, with support from the exposure/risk information, "recognizing the uncertainties attendant with both," in addition to public comment and supporting advice from the CASAC (81 FR 71935, October 18, 2016).

In both the 2008 and 2016 reviews, a range of additional uncertainties, limitations, and assumptions related to the 2007 REA modeling was described (see 2007 REA section Appendix M, Exhibit M-1 and 2011 REA Planning Document, Table 2-3). These sources of uncertainty occur in the different modeling steps, as briefly summarized here, with some additional detail provided in Table 2-3 below.

- *Characterizing ambient air Pb levels.* Unlike the other sources of uncertainty discussed in the bullets below that apply to both the generalized local and location-specific case studies, uncertainty related to air quality characterization differs between these two case studies. Uncertainty related to the characterization of ambient air Pb levels is contributed by several elements of this modeling step including:
    a) characterization of spatial gradients in ambient air Pb levels in the location-specific urban context using monitoring data *[location-specific element]*;
    b) characterization of single exposure zone without spatial gradients in ambient air Pb levels in the general near-source case study) *[generalized local element];*
    c) conversion of air quality metric associated with the standard and potential alternatives of interest to an equivalent annual average Pb concentration for the blood Pb modeling time step (e.g., maximum quarterly or monthly averages were converted to annual average concentrations utilizing ratios reflecting relationships in ambient air monitoring data) *[element for both]*; and
    d) simulation of air quality patterns differing from what were current in the location specific case studies (using a proportional rollback across monitor sites, a pattern that may differ from what would occur based on actual implementation strategies) *[location-specific element]*.
- *Characterizing Pb concentrations in indoor residential dust*. Given the potential importance of the indoor residential dust pathway to ambient air Pb-related exposure, it is addressed separately from the other media. The hybrid *(mechanistic-empirical)*

indoor dust Pb model combines mechanistic (compartmental) modeling elements with empirical (survey-statistical) data to simulate the relationship between outdoor ambient air Pb and Pb in indoor dust (with consideration for non-air contributions such as the tracking in of outdoor soil Pb, which may have derived from nonair sources, and paint Pb). A number of aspects of the hybrid model are potential sources of uncertainty (e.g., cleaning frequency and efficiency, Pb deposition and air exchange rates, treatment of Pb resuspension indoors, handling of non-air related indoor dust Pb fraction, empirical regression equations used to convert loadings to concentrations).

- *Characterizing Pb exposure from the multiple pathways*. The approaches for representing Pb exposures from sources not identified above were also subject to various sources of uncertainty, including:

  (a) estimates (and their supporting data) used for exposure related to drinking water ingestion, dietary Pb, and incidental ingestion of indoor dust and outdoor soil;

  (b) the approach for deriving inhalation-exposure concentrations of ambient air Pb; and

  (c) the use of constant, unchanging Pb concentrations in all exposure media for the 7-year exposure modeling period (e.g., assumption of same residence and unvarying annual average media concentrations).

- *Estimating blood Pb levels for 7-year old children (resulting from seven years of exposure since birth).* The IEUBK model was used to estimate mean blood Pb levels (with which an empirically derived GSD was used to derive population distribution of blood Pb levels). The IEUBK model application was subject to a number of sources of uncertainty including specification of absorption factors for dietary and drinking water Pb and for indoor dust Pb. There was also uncertainty related to the limitations in the extent to which IEUBK performance for the REA exposures (and the specific mix of pathways) had been evaluated and assessed. Uncertainty may also be contributed by the GSD used to characterize interindividual variability in blood Pb to the extent it is not representative of the population being modeled in the REA.

- *Estimating risk (IQ decrement) for young children*: There are a number of sources of uncertainty associated with specification and application of the C-R functions derived from the Lanphear et al. (2005) pooled analysis for the scenarios modeled. These include: (a) the potential for covariates on the Pb effect to not have been fully accounted for in the model; (b) potential differences between the Lanphear et al. (2005) pooled study population and the populations in the REA case studies; and (c) application of the C-R functions at levels at or below the lowest blood Pb levels in Lanphear et al. (2005).

2.2 KEY CONSIDERATIONS

Our planning for an REA in this review involves a number of considerations related to the design and application of the 2007 REA in supporting both the 2008 and 2016 Pb NAAQS reviews. We begin in section 2.2.1 by considering sources of uncertainty impacting the 2007

REA, noting those areas where newer information or data could result in refinements to the REA to increase overall confidence in the analyses. Next in section 2.2.2, we consider the way in which the REA was used in informing the 2008 and 2016 NAAQS reviews, including implications for the design of the REA going forward. And finally, in section 2.2.3, we consider the extent to which more recently available data and information support the assessment of health effects associated with Pb, other than IQ decrements, and/or assessment of exposure/risk to other age-groups and lifestages.

As discussed in section 2.1, there are a variety of complexities associated with the assessment of air-related Pb exposure and health risk. In designing the REA to support the current review, as was done in the 2008 review, we have attempted to focus effort on those aspects that are most important and feasible to address within our scope and given the constraints of time, pertinent data, models, etc. The conceptual model for current REA planning is presented in Figure 2-4, with shaded boxes indicating items to include in modeling for the REA for which ambient air has played a role (note, sources in the hatched boxes, while not directly linked to ambient air Pb, would also be reflected in the modeling of exposure/risk). The conceptual model presented in Figure 2-4 is intended to facilitate consideration of design aspects important to planning for an REA, including in particular the discussion of uncertainties identified in the 2007 analysis and the degree to which more recent data and information allow us to address those uncertainties, thereby supporting the design of an updated and refined REA.

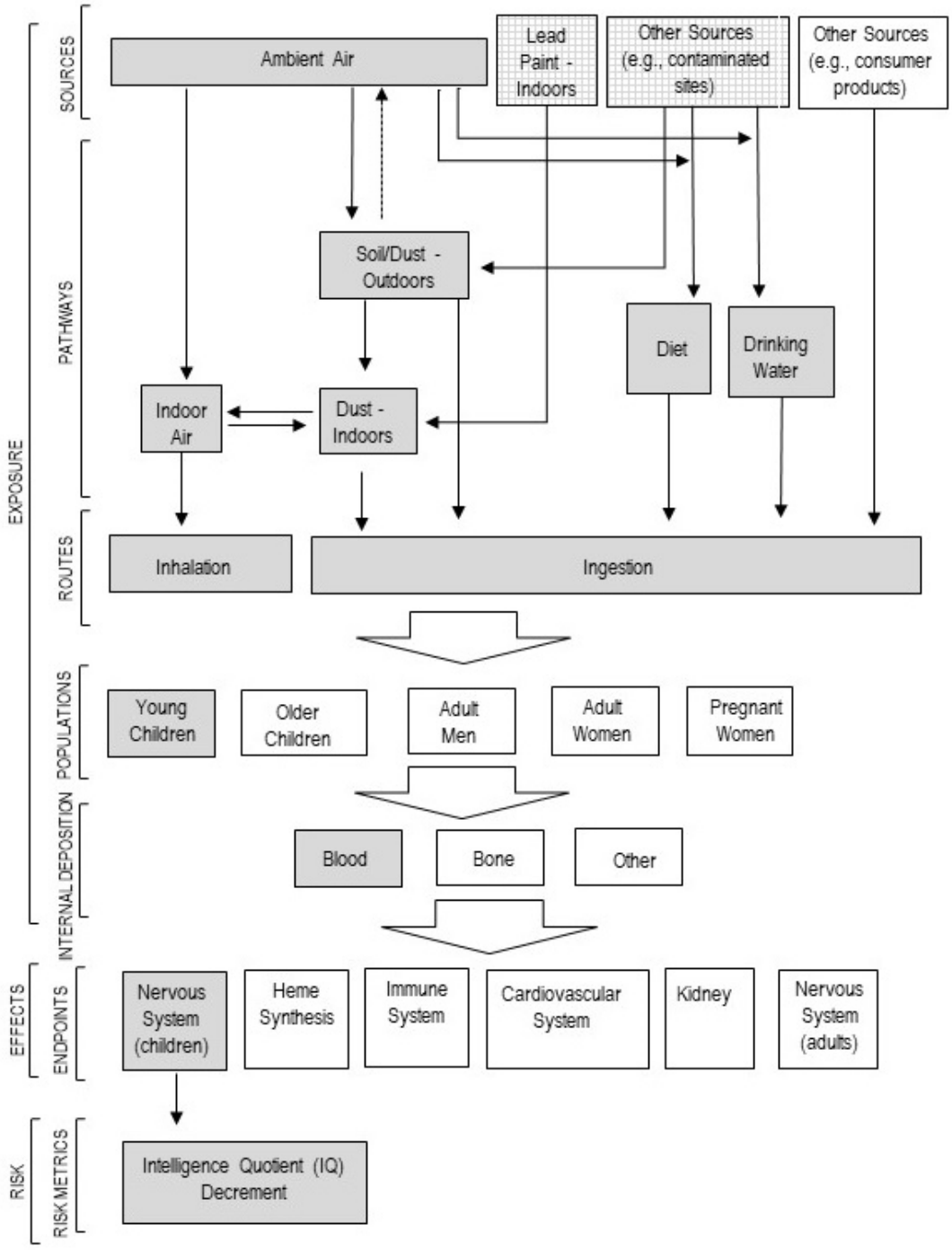

Figure 2-4. Conceptual model for 2007 Pb human health risk assessment.

2.2.1 Newly Available Information Regarding Key Limitations or Uncertainties of 2007 REA

An important factor in considering an update to the exposure/risk assessment is the degree to which new information available since the 2007 REA allows us to address key sources of uncertainty, thereby resulting in an updated REA model with greater overall confidence. This question was explored in the previous Pb NAAQS review completed in 2016 with the conclusion being, at that time, that newly available information would not substantially improve the utility of risk estimates in informing the current Pb NAAQS review (see 2011 EPA planning document, section 2.3). Section 2.1.3 above identifies key limitations and uncertainties associated with the exposure/risk estimates in the 2008 and 2016 reviews. In our consideration here of the currently available information, while we focus on the period since the last Pb NAAQS review, we also consider the full array of information available since development of the original REA in 2007.

We have performed a detailed assessment of the newly available information in the context of its potential for addressing sources of uncertainty in the exposure and risk estimates. That assessment is summarized in Table 2-3. The model design elements for which there is newly available information that could contribute to more up-to-date estimates, , are described below and it is these technical areas that would be updated or refined in the context of new exposure and risk analyses as part of the current review.

- *Converting the air quality metric for the current standard to an annual-average concentration reflecting recent patterns in daily air Pb monitoring data for use in modeling exposure and risk:* While information published since the 2007 REA does not allow us to reduce uncertainty associated with this conversion step, more recent monitoring data are available that can be used to generate more updated ratios for use in these conversions.
- *Modeling relationship between outdoor ambient air Pb and indoor residential dust Pb using hybrid (mechanistic-empirical) model*: The hybrid indoor dust Pb model is a critical element of the 2007 REA and allowed the impact of recent ambient air Pb on indoor dust Pb to be evaluated through the associated fate and transport pathway (the loading of indoor residential dust Pb by outdoor ambient air Pb). Newer information may allow important components of the hybrid model to be updated, including the approach used to convert dust Pb loadings to concentrations as well as the air exchange rates (AERs) between outdoor air and indoor air. The availability of AER data that may be specific to different cities or regions of the country and for specific types of housing (e.g., those with and without air conditioning) may allow customization of the model for different regions of the country and different types of housing. This could increase overall confidence in the model by enhancing the representativeness of the model for locations likely to experience disparities in indoor dust Pb loading per unit of outdoor ambient air Pb.
- *Characterizing exposure to Pb through drinking water and dietary ingestion and incidental outdoor soil ingestion*: As noted earlier, assessment of air-related Pb

impacts requires consideration for the multi-pathway nature of Pb exposure in order to estimate total Pb exposure. In the development of an updated assessment, we would anticipate updating the characterization of Pb in media with data published since the 2007 REA. This will include consideration of estimates for urban/residential soil and diet and drinking water based on recent evidence described in sections 2.1.3.2 and 2.1.3.3, respectively of the draft ISA. In addition, we will consider the currently available data on background Pb concentrations in drinking water and dietary sources as well as updated exposure factors utilized in IEUBK 2.0 (U.S. EPA, 2021a).

- *Modeling blood Pb levels in young children given pathway-specific intake estimates utilizing IEUBK*: Presuming use of an IEUBK-based approach to modeling exposure for children from birth up to age seven years, as in the 2007 assessment, we note that, while IEUBK has not been significantly refined since the 2007 REA, some of the exposure factors (intake rates) have been updated. In addition, performance evaluations have been completed for IEUBK by the EPA since the 2007 REA that have focused on the ability of the model to evaluate a target 95th percentile blood Pb level of 5 µg/dL (draft ISA, Appendix 2, section 2.6). Findings from these evaluations may inform characterization of the range of exposures over which the IEUBK model can be utilized without appreciable extrapolation and therefore the level of exposure below which there is increased uncertainty in modeling exposure/risk. This type of performance-based analysis of confidence represents an improvement over the uncertainty characterization for modeled exposure and risk in the 2007 REA, and, thus, could be an important refinement for an updated analysis.
- *Characterizing variability in blood Pb levels using empirically derived GSDs*: Presuming use of IEUBK to estimate a central-tendency blood Pb value for a study population coupled with an empirically derived GSD to characterize variability in blood Pb levels around that central tendency value, we recognize the availability of additional blood Pb datasets that may provide for updating the GSD. For example, blood Pb data from more recent studies for child populations of similar age to those modeled in the REA may provide for estimation of variability reflecting generally lower blood Pb levels common in the more recent years. We would anticipate that GSDs for a smaller population of children in the residential context may have changed from those utilized in the 2007 REA given the declining trends in overall blood Pb levels that include smaller subsets of children continuing to experience relatively higher blood Pb levels (section 1.3.2 above; draft ISA, Appendix 2, section 2.4.1).
- *Modeling IQ decrement in young children*: Given the backdrop of declining blood Pb levels in young children in the U.S., we anticipate that the IQ risk modeling would focus on a lower range of blood Pb levels than those in the 2007 REA (i.e., in the range of 5 µg/dL and below).[17] While there have been a number of studies published since the 2007 REA assessing associations of children's IQ with children's blood Pb

[17] Although the 2007 REA did not estimate blood Pb for an air quality scenario just meeting the standard that was adopted in 2008, it estimated blood Pb for a somewhat similar scenario. In the generalized local (then called general urban) case study, with its simplifying assumptions, the estimated blood Pb levels for the scenario based on a mean maximum quarterly average of 0.14 µg/m^3 were 2 µg/dL (median total blood Pb) and 4 to 7 µg/dL (total blood Pb at the 95th percentile) (see 2007 REA, section 3.4, Tables 3-7). Thus, a focus on risk associated with blood Pb levels at and below 5 µg/dL is a reasonable expectation for this review.

(e.g., Haynes et al., 2015, Martin et al., 2021), for reasons summarized in Table 2-3, none of these studies provides support for C-R functions for this REA application. However, given the current lower range of blood Pb levels, consideration of a different approach from that used in the 2007 REA is appropriate. Rather than a focus on the array of C-R extrapolations (to the blood Pb levels of interest) from the nonlinear models presented in Lanphear et al. (2005), with corrections of Lanphear at al. (2019), we are considering an approach focused on linear models for studies involving narrower and lower blood Pb distributions, including the lower blood Pb subset of studies included in the Lanphear et al. (2005) pooled dataset. For example, the studies of child populations in Rochester, NY, and Boston, MA, contributed the majority of lower blood Pb observations in the pooled dataset. We would look to analyses of the association of IQ with blood Pb for these groups of children (e.g., Lanphear et al., 2005 with corrections of Lanphear at al. 2019, Figure 2; Canfield et al., 2003; Bellinger, 2003) to identify C-R functions that may be appropriate for assessing risk of IQ decrements at these lower blood Pb levels. In Lanphear et al. (2005), non-linear functional forms were utilized to capture the steeper unit risk associated with the lower blood Pb levels in the pooled dataset (e.g., below 7-10 µg/dL) while also describing the less steep relationship across the higher Pb levels in the dataset (e.g., 95th percentile of 35.7 µg/dL, concurrent). For our focus on characterizing risk for children with Pb levels only within the lower end of the range (at/below approximately 5 µg/dL), the nonlinear form is not needed and there would be lower uncertainty with risk estimates based on the linear C-R functions from analyses for that blood Pb range.

Table 2-3. Assessment of information (including methods and models) newly available in this review related to quantitative assessment of exposure and risk of IQ decrements in children.

Modeling Dimension	Uncertainty Related to Application in 2007 REA	Newly Available Information and Assessment of Utility in Informing Update of REA Model
Characterizing Ambient Air Pb Levels (current conditions, current standard, and alternative standards)		
A) Characterizing spatial gradients in ambient air Pb levels in the urban context. For the location-specific urban case studies (including study areas based on Chicago, Cleveland and Los Angeles), spatial variation in ambient air Pb levels was characterized using ambient air Pb data for all monitors within each study area, which were defined as the portion of each city within one mile of an existing urban monitor. U.S. Census blocks were used as the basic unit of analysis with each block being assigned the source-oriented monitor closest to it (if that monitor was within a mile of the block centroid) or the nearest non-source oriented monitor. Interpolation of monitor data in this fashion allowed a degree of spatial gradient in monitored ambient air Pb levels to be reflected in risk modeling (including the intersection of that ambient air Pb gradient with demographics characterized at the block-level). Conversely, for the generalized local case study, a simpler approach was used. Here, it was assumed that a relatively smaller group of children (e.g., a smaller neighborhood or residential area) existed in a very small area within which there was a uniform ambient air Pb level. This approach avoided the need for any interpolation or direct use of monitoring data.	Limitations in our monitoring network and in studies of smaller scale spatial gradients in ambient air Pb levels in the urban setting introduced uncertainty into our characterization of exposure levels and risk for residential populations modeled for the location-specific urban study areas. Similarly, limitations in our characterization of ambient air Pb levels more generally prevented us from identifying areas across the U.S. with the attributes associated with the generalized local study area which could have their exposure/risk represented by the generalized local case study scenario. In the 2007 REA both of these sources of uncertainty were assessed to have a *particularly significant impact* on the risk estimates generated (see 2007 REA Appendixes, Appendix M, Exhibit M-1).	Evidence from studies published since the 2007 REA suggests that there continues to be substantial intra-urban variability in ambient air Pb levels with elevated levels being associated with proximity to specific sources (and often captured by source-oriented monitors), while lower levels are often associated with more generalized urban areas. However, the monitoring network in place is generally not refined enough to provide comprehensive coverage for an urban area such that the nature of the spatial gradient can be well-characterized on a more localized (neighborhood) level (draft ISA, section IS2.6; 2013 ISA, section 2.5.1.2). Lead emissions and concentrations in the U.S. continue to steadily decline with major industrial sources having either reduced their emissions or closed, resulting in the emergence of aviation gas as the dominant contemporary source (draft ISA, Appendix 1, section 1.6). This information suggests that the currently available information does not provide the detailed information on gradients that would be needed to reduce uncertainty associated with this modeling element.

Modeling Dimension	Uncertainty Related to Application in 2007 REA	Newly Available Information and Assessment of Utility in Informing Update of REA Model
B) Simulating air quality scenarios of interest (e.g., meeting existing and, as appropriate, potential alternate standards). For the location-specific urban case studies, the simulation of air quality scenarios of interest was achieved using a proportional adjustment approach, i.e., each monitor value for the exposure metric under consideration was adjusted by the same proportion needed for concentrations at the design monitor to just meet the existing standard or potential alternate of interest (in terms of the standard averaging time, level and form) (2007 REA Appendices, Appendices C and O). For the generalized local case study, the constant air concentration was set equal to the existing standard or potential alternate of interest (in terms of the standard averaging time, level and form).	There is uncertainty associated with the use of proportional rollback to simulate meeting the air quality scenarios of interest since measures taken to meet specific standards could result in ambient air Pb reductions that diverge from proportionality across the study area.	This element remains a source of uncertainty for location-specific case studies. The simplifying assumption of a lack of gradients in the generalized local case study contributes a different type of uncertainty (as noted earlier).
C) Converting air quality metrics (associated with the standard of interest) to an equivalent annual-average to use in modeling exposure and risk. Modeling of exposure and risk in the 2007 REA utilized annual-average Pb levels and consequently air metrics associated with standards of interest (e.g., max quarterly, max monthly) had to be converted to the annual averages associated with the air quality scenarios for the various metrics. This was done with ratios based on ambient air monitoring data. These ratios were the mean or 95th percentile ratio of the metric to the annual average for the same location and time period for monitors from urban areas with at least a million people, in order to reflect ambient air Pb trends in larger urban locations.	There is uncertainty introduced into the analysis by these ratios (2007 REA Appendices, Appendix O, Exhibit M-1).	While information published since the 2007 REA does not allow us to reduce uncertainty associated with the generation or application of these ratios, the fact that ambient air Pb concentrations have changed substantially since that time suggests that at the very least, these ratios should be updated to reflect more recent ambient air Pb concentrations across urban areas.

Modeling Dimension	Uncertainty Related to Application in 2007 REA	Newly Available Information and Assessment of Utility in Informing Update of REA Model
Characterizing Pb concentrations in indoor residential dust (given the importance of this exposure pathway in the context of ambient air Pb-related exposure it is addressed here separately from the other media)		
D) Modeling relationship between outdoor ambient air Pb and indoor residential dust Pb using hybrid (mechanistic-empirical) model. The 2007 REA utilized the hybrid indoor dust Pb model which combined (a) an empirical (compartmental) modeling to relate outdoor ambient air Pb to the loading of indoor dust Pb and (b) empirical data obtained from the U.S. Housing and Urban Development [HUD] National Survey of Lead-based Paint in Housing (U.S. EPA, 1995) to characterize the other contributions to indoor dust Pb (e.g., tracking of outdoor soil/dust indoors, indoor paint flaking, etc.). Empirical (regression) relationships were then used to convert estimates of indoor dust Pb loading to concentrations required for IEUBK blood Pb modeling (see 2007 REA, section 3.1.4.1 for additional detail on the hybrid indoor dust Pb model).	A number of elements of the hybrid indoor dust Pb model and its application were identified in the 2007 REA as having *particularly significant impacts* on risk estimates including: (a) estimates of cleaning frequency and efficiency, (b) potential variability in the Pb deposition and air exchange rates, (c) failure to consider Pb resuspension indoors (which could bias the indoor dust Pb levels high), (d) characterization of non-air related indoor dust Pb fraction using HUD data, and (e) empirical (log-log regression) equations used to convert loadings to concentrations (2007 REA Appendixes, Appendix M, Exhibit M-1).	A number of new studies are available since the 2007 REA, with data potentially addressing uncertainties related to the hybrid indoor dust Pb model. These include: (a) Hunt et al., (2008) which examined the efficiency of vacuuming in removing Pb dust from household surfaces and reported updated cleaning efficiency estimates for vacuuming hard floors (lack of information for other types of indoor surfaces, including carpets, may limit its potential to reduce overall uncertainty) and (b) Bevington et al. (2021) which addressed the conversion of indoor dust Pb (wipe) loadings to concentrations utilizing a large pooled dataset and generating 17 regression models for converting loadings to concentrations. In addition, data now available on air exchange rates may support an update to that aspect of the model. These data (Cohen and Rosenbaum, 2012) have been most recently used by EPA to update inputs to the Air Pollutant Exposure (APEX) model for use in the exposure assessment in the 2020 ozone NAAQS review (U.S. EPA, 2020, Appendix 3D, section 3D.2.6.1.1). The availability of these new studies (particularly Bevington et al., 2021) indicates the potential for updates that may contribute to reduced uncertainty in estimates of dust Pb concentration from that in the 2007 REA.
E) Modeling relationship between outdoor ambient air Pb and indoor residential dust Pb using an air-only regression model. In addition to the hybrid indoor dust Pb model described above, in the 2007 REA, indoor dust Pb was also estimated using an air-only regression model obtained from the literature (U.S. EPA,	2007 REA Appendixes, Appendix M, Exhibit M-1 addresses uncertainty associated with the regression-based (air-only) model noting that several of the locations included in the data used to generate the model were in urban environments, but the data were	No new studies characterizing the empirical (statistical) relationship between ambient air Pb and indoor residential dust Pb were identified since the 2007 REA. EPA notes that section 1.3.4 of Appendix 1 of the draft Pb ISA focuses on the important issue of resuspension of legacy Pb in urban soil as a source of ambient air Pb but does not discuss any research addressing the empirical relationship between

Modeling Dimension	Uncertainty Related to Application in 2007 REA	Newly Available Information and Assessment of Utility in Informing Update of REA Model
1989). That model estimates indoor dust Pb based on (a) outdoor ambient air Pb (multiplied by an air-related factor) and (b) an intercept which captures other impacts besides air (e.g., indoor paint). The air factor used in this equation is expected to capture longer-term impacts of outdoor air Pb on indoor dust, including the indirect effect of air Pb on outdoor soil/dust Pb with subsequent impacts of that outdoor soil/dust Pb on indoor dust Pb through other mechanisms (U.S. EPA, 1989).	dominated by point sources. Thus, this equation's application in urban environments is limited by the representativeness of the locations included in the original pooled analysis and the extent to which current conditions are represented by conditions in the 1980s when the data were collected (noting in particular that ambient air Pb levels have decreased substantially as have direct emissions of Pb into the ambient air). It is unclear how these uncertainties may bias the estimated indoor dust Pb concentrations.	ambient air Pb (whether new sourced or entrained) and the buildup of Pb in indoor dust.
Modeling multi-pathway Pb exposure (estimation of the indoor dust Pb covered separately – see above)		
F) Characterizing exposure to Pb through drinking water and dietary ingestion and incidental outdoor soil ingestion. Note, indoor dust and inhalation of outdoor/indoor air addressed separately – see D and E for the former and G for the latter. Exposure estimates for these pathways used as IEUBK inputs were estimates for the central tendency of the U.S. population.	These inputs may contribute uncertainty to the blood Pb estimates associated with a number of factors: (a) the potential for specific urban areas to have media concentrations that diverge from the central-tendency values used in the analysis, (b) the possibility that the exposure factors utilized may not reflect the central tendency for all children including, particularly, disadvantaged children, (c) regarding drinking water estimate, the potential for the estimate to under-represent Pb concentrations in drinking water from older housing that could be more impacted by Pb piping (2007 REA Appendixes, Appendix M, Exhibit M-1).	Newer study data characterizing Pb concentrations in relevant media have been published since the 2007 REA. For example, for newer estimates for urban/residential soil (draft ISA, Appendix 2, section 2.1.3.2), and newer data for dietary items including drinking water (draft ISA, Appendix 2, section 2.1.3.3). These more recent data across both Pb media concentrations and exposure factors would be consulted to update the method for modeling multi-pathway Pb exposure.

Modeling Dimension	Uncertainty Related to Application in 2007 REA	Newly Available Information and Assessment of Utility in Informing Update of REA Model
(G) Characterizing Pb exposure concentrations. The estimation of the Pb exposure concentrations for children that reflect time spent indoors versus outdoors was completed using location-specific adjustment factors also used in the exposure modeling component of EPA's 1999 national-scale air toxics assessment (U.S. EPA 2006c) (see 2007 REA section 3.1.2).	The adjustment factors used in the 2007 REA for exposures from birth through age 7, which modeled exposure from birth through age 7, were those used in the exposure modeling for EPA's 1999 air toxics assessment for the 0-4 year-old age groups, which introduced uncertainty into these estimates. Additionally, the penetration factor utilized in the derivation of the adjustment factorto estimate fraction of outdoor air Pb that reaches indoor air is based on another particulate metal compound, hexavalent chromium, which is more reactive than Pb, potentially introducing uncertainty into use of the factors for Pb. Furthermore, the mean for the penetration factor was used for all modeled individuals which masks potential variability in this outdoor-to-indoor Pb ratio across individuals (for further discussion of these sources of uncertainty see 2007 REA, Appendix M, Exhibit M-1).	No more recent analyses of this issue or outdoor to indoor Pb concentrations is available.
H) Pathway apportionment of modeled blood Pb levels (and risk) for different population percentiles of interest at a given study area (reflecting assumption regarding potential correlation of Pb exposure across exposure pathways). A critical step in modeling risk for the 2007 REA was the pathway apportionment of both exposure and risk for specific percentiles of a simulated population. Given the relative lack of data characterizing correlations among exposure pathways at the population level to inform a more	There is appreciable uncertainty associated with this element as, in reality, the relative roles of different pathways might be expected to shift with higher exposure percentiles (e.g., Pb paint and/or drinking water exposures may increase in importance, with air-related contributions decreasing as an overall percentage of blood Pb levels) The 2007 REA identifies this source of uncertainty as	While several studies have used data from the EPA-sponsored National Human Exposure Assessment Survey (NHEXAS) dataset to characterize potential correlations between Pb in potential media of interest including indoor air, drinking water, indoor dust and outdoor soil (draft ISA, Appendix 2, section 2.1.3; Clayton et al., 1999; Egeghy et al., 2005), these analyses focus on media concentrations and do not provide correlation information regarding percentiles of relevant intake rates (exposure factors) for children which would be needed to characterize potential correlations

Modeling Dimension	Uncertainty Related to Application in 2007 REA	Newly Available Information and Assessment of Utility in Informing Update of REA Model
refined approach, the central-tendency pathway apportionment was applied to all modeled blood Pb percentiles (i.e., the fraction of total blood Pb associated with recent air-source indoor dust ingestion for the average child was also the fraction for the 90th and 95th percentile modeled child).	assessed to have a *particularly significant* impact on the risk estimates generated in the 2007 REA, Appendix M, Table M-1).	between exposure pathways across percentiles of a modeled child population.
Estimating Blood Pb Levels for Children (0-7 years of age)		
I) Modeling blood Pb levels in young children given pathway-specific intake estimates utilizing IEUBK. In the 2007 REA, the IEUBK model was used to estimate mean blood Pb levels for a given scenario. A subsequent step (addressed below) involved the use of an empirically-derived GSD to characterize population-level variability in blood Pb levels around that mean blood Pb estimate.	Although limited data were available in 2007 for performance evaluation, the IEUBK estimates were observed to be similar to data reported in the 2006 AQCD for children with known Pb exposure (see 2007 REA, Appendix J, section J.1 for additional detail). The 2007 REA further identifies potential uncertainty associated with the soil/dust and indoor dust GI absorption factors that were used in IEUBK modeling (i.e., diet and drinking water = 0.50, outdoor soil/dust and indoor dust = 0.30) in light of the wide variation across the estimates (2007 REA, Appendix M, Table M-1 and Appendix H, Table H-6). The 2007 REA concludes that these estimates may either over- or under-estimate the actual GI absorption for a child in these study areas, with this factor having a *particularly significant* impact on risk estimates (2007 REA, Appendix M, Table M-1).	The information newly available since the 2007 REA includes an updated IEUBK model (v2.0) which has been evaluated in the context of estimating exceedance of target 95th percentile blood Pb of 5 µg/dL (draft ISA, Appendix 2, section 2.6). This performance evaluation was completed using children's blood Pb data paired with Pb concentrations for yard soil and indoor dust (U.S. EPA, 2021b). A consideration in an updated application of the IEUBK model would be the extent to which blood Pb estimates in the application fall into lower concentrations than those assessed in the performance evaluation, representing an extrapolation beyond the evaluated performance of the model and accordingly contributing increased uncertainty to the estimates. The current version of IEUBK (2.0) includes updated exposure factors for some of the exposure pathways involved on total blood Pb modeling (U.S. EPA 2021a, section 2.3.1.6; U.S. EPA, 2018a; U.S. EPA, 2018b; U.S. EPA, 2018c; U.S.EPA, 2018d). Those updated factors, and the associated evidence, will be considered in any future simulations of exposure and blood Pb levels conducted using the model.
J) Characterizing variability in blood Pb levels using empirically derived GSDs. The IEUBK-generated mean blood Pb estimate (for each	The extent to which the population on which the GSD is based differs from the population that is the focus of risk	Since the 2007 REA, blood Pb levels in children have continued to decrease over time (draft ISA, Appendix 2, section 2.4.1), although the extent to which population

Modeling Dimension	Uncertainty Related to Application in 2007 REA	Newly Available Information and Assessment of Utility in Informing Update of REA Model
scenario) was combined with a GSD representing variability around that mean estimate for children from a hypothetical population whose Pb exposures are similar. The GSD encompasses biological and behavioral differences, measurement variability from repeat sampling, variability as a result of sample locations, and analytical variability (U.S. EPA, 2021a, section 2.3.8).	modeling in a particular study area contributes uncertainty to the estimates (2007 REA, Appendix M, Table M-1). At the time of the 2007 REA, the data seemed to indicate a trend of higher population-level GSDs in more recent datasets even as overall blood Pb levels in children decreased (possibly reflecting the fact that a subset of individuals were being left higher up on the blood Pb distribution perhaps due to artifact Pb exposure even as general Pb exposure levels decreased), also potentially contributing uncertainty to the estimates (2007 REA, Appendix M, Table M-1). The GSDs for the 2007 REA were obtained from studies of blood Pb variability in specific populations and can display considerable variation reflecting a number of factors which can introduce uncertainty (e.g., population and geographic size, spatial variation in Pb levels for key media, differences in housing attributes or behavior of the children).	variability (as summarized by a GSD) has changed is not clear. More detailed analysis of the currently available information may indicate whether GSDs associated with more recent child population blood Pb datasets have shifted (e.g., along with the general decreasing trend in blood Pb levels). Since the 2016 review, an additional population-level blood Pb modeling approach has been developed by EPA that utilizes a reduced form of IEUBK in combination with the Stochastic Human Exposure and Dose Simulation (SHEDS) multimedia model. This approach, rather than applying a GSD to the mean blood Pb level estimated for a specific age (based on a multi-year exposures to mean concentrations for all relevant exposure media/pathways), applies stochastic sampling to media concentrations and exposure parameters to develop pathway-specific Pb intake rates for each simulated child which are in turn translated into total blood Pb estimates (Zartarian et al., 2017). Although the SHEDS-IEUBK approach is valuable for multiple applications, several aspects of the analytical design described in this document lead us to continue to identify the GSD-based approach for simulating exposure variability as appropriate to this assessment. For example, the current analytical design for this REA is not focused on a large-scale population assessment. Rather, it focuses on small (neighborhood-scale) groups of children living in localized areas with ambient air concentrations equal to the standard of interest. Also, the GSD approach proposed here avoids the potential for added uncertainty associated with characterizing potential correlations between exposure factor distributions (which is required for the accurate simulation of high-end exposure using probabilistic methods such as the SHEDS-IEUBK approach).

Modeling Dimension	Uncertainty Related to Application in 2007 REA	Newly Available Information and Assessment of Utility in Informing Update of REA Model
Estimating Risk for Young Children		
K) Modeling IQ decrement in young children. For the 2007 REA, IQ decrement was estimated using several C-R functions derived from statistical models of IQ association with blood Pb reported in Lanphear et al. (2005). These functions each involved different approaches to estimating IQ decrement at and below the lowest blood Pb measurements in the Lanphear et al. (2005) pooled dataset: (a) log-linear function with a cutpoint at 1.0 µg/dL concurrent, (b) log-linear function with low-dose linearization, (c) dual-linear with stratification at 10 µg/dL peak BLL and (d) dual-linear with stratification at 7.5 µg/dL peak BLL (for additional detail on these C-R functions see 2007 REA, section 5.3.1.1).	While any effects of covariates on the Lanphear et al. (2005) model predictions are unknown, given that the IQ change functions used in this analysis were derived from this Lanphear study, any inherent differences between the Lanphear et al. (2005) populations and the children simulated in the 2007 REA case studies contribute uncertainty to the associated IQ estimates (2007 REA Appendix M, Table M-1). The 2007 REA also highlights as a *particularly significant* source of uncertainty, in terms of its potential impact on risk, estimates of the degree of health decrement associated with lower exposure levels (i.e., blood Pb levels less than 5 µg/dL). This magnitude of blood Pb levels were represented in only a small minority of the Lanphear et al (2005) pooled dataset. Accordingly, estimates for these blood Pb levels based on the nonlinear function (which was intended to capture the steeper unit risk associated with the lower blood Pb levels in the dataset (e.g., below 7-10 µg/dL) while also describing the less steep relationship across the higher Pb levels in the dataset (e.g., 95th percentile of 33.2 µg/dL) have increased uncertainty. The array of estimates produced by the four blood Pb-IQ functions used provide an	Consideration of the currently available information for this modeling element focuses on risk of IQ decrement impacts at the generally lower blood Pb levels associated with current exposures and the existing standard. As at the time of the 2013 review, the recently available evidence does not include new studies of blood Pb and IQ that fit our needs with regard to a study of blood Pb and IQ in U.S. children with blood Pb levels similar to those common in the U.S. today. The current draft ISA makes this point, stating in the executive summary (draft ISA, section ES.7.1.3) that: "The evidence assessed in the 2013 Pb ISA found that cognitive effects in children were substantiated to occur in populations with mean BLLs between 2 and 8 µg/dL. Recent studies generally include somewhat older children or employ modelling strategies designed to answer relatively narrow research questions and consequently do not have the attributes of the studies on which the conclusion of the 2013 Pb ISA was based (i.e., early childhood BLLs, consideration of peak BLLs, or concurrent BLLs in young children). Therefore, the recently available studies were not designed and may not have the sensitivity to detect the effect or hazard at these very low BLLs, nor do they provide evidence of a threshold for the effects across the range of BLLs examined." For that reason, in considering evidence available for modeling IQ decrement in younger children, we look back to epidemiology studies utilized as the basis for risk modeling in the 2007 REA. Although the set of C-R functions derived from Lanphear et al. (2005) and used in the 2007 REA provided different approaches for extrapolating from the loglinear model based on the pooled dataset to blood Pb levels generally below those in the dataset, the vast majority of the observations in the pooled analysis occur at exposures above our range of potential interest, such that the fitting of the initial log-linear

Modeling Dimension	Uncertainty Related to Application in 2007 REA	Newly Available Information and Assessment of Utility in Informing Update of REA Model
	illustration of this uncertainty (2007 REA Appendix M, Table M-1).	form may be dominated by data outside (above) our range of interest. Several errors were identified in the original pooled analysis of Lanphear et al. 2005 and subsequently corrected (Lanphear et al. 2019, Crump et al. 2013, Kirrane and Patel 2014). In addition, Crump et al. (2013) extended the original analysis by employing different approach to the log transformation of BLL and a modelling strategy that was designed to use more of the available data. The alternative analysis of Crump et al. (2013) supported the findings of the original analysis. However, rather than relying on the analyses of the international pooled dataset of Lanphear et al. (2005), corrected in Lanphear et al. (2019), with its heavy representation of blood Pb levels higher than those of interest, another approach would be to consider a C-R function based on analyses of the association of IQ with blood Pb for the cohorts that had contributed to the majority of lower blood Pb levels in the Lanphear et al. (2005 dataset), as corrected in Lanphear et al. (2019), i.e., the Rochester, NY and Boston, MA cohorts (e.g., Lanphear et al., 2005, Figure 2; Canfield et al., 2003; Bellinger 2003). This focus on C-R functions from studies with Pb exposure closer to the range of interest in this review (5-7 µg/dL and below) will increase confidence in the associated risk estimates. We have focused on U.S studies to reduce uncertainty that can result from a mismatch between attributes of the epidemiology study population (e.g. potential confounders, effect modifiers and behavioral factors related to Pb exposure) and the U.S. population that is the focus of the Pb NAAQS risk assessment. The other studies of children in the U. S. released since completion of the 2007 REA focusing on association of IQ with Pb exposure vary in terms of specific factors that may compromise their appropriateness as a basis for C-R functions to predict IQ decrements

Modeling Dimension	Uncertainty Related to Application in 2007 REA	Newly Available Information and Assessment of Utility in Informing Update of REA Model
		associated with Pb in the context of risk modeling. For example, while Chiodo et al. (2007) examines IQ associations with blood Pb of a child cohort in Detroit, the results may less generalizable than the Rochester or Boston cohorts due to high prevalence of prenatal alcohol and drug use (2013 ISA, Table 4-3). A number of more recent studies have considered the effects of Pb co-exposure with manganese (Mn) on children near an industrial facility in the vicinity of East Liverpool Ohio (Haynes et al., 2015; Martin et al., 2021). The study population is considerably older than the 0-7 yr age range that is the focus of IEUBK-based blood Pb modeling used in the 2007 REA. Modeling of exposure and risk for such older child populations (e.g., children older than seven years, including teenagers) is subject to increased uncertainty both with regard to the timing, and other aspects of the exposures that may be influencing the outcomes with which blood Pb levels are associated and regarding the simulation of exposure patterns and associated blood Pb levels for these older cohorts. In addition, while these studies have found associations between Pb exposure and IQ the presence of elevated Mn exposure reduces the generalizability of these results to other populations.

An overarching limitation of the 2007 REA concerned parsing out blood Pb and risk estimates specific to air-related Pb. As noted earlier, in light of this, we presented air-related estimates in terms of upper and lower bounds. We note that the newly available information does not provide for a reduction in the uncertainty associated with parsing out blood Pb and risk estimates specific to air-related Pb.

2.2.2 Consideration of Other Health Endpoints and/or Population Age Groups/Life Stages

Another aspect to evaluation of information newly available since the 2007 REA is the consideration of support for quantitative assessment of risk of health effects other than IQ decrements and/or risk to other ages or life stages. In the planning phase of the 2016 review, the 2011 REA Planning Document considered specific endpoints other than IQ decrements and ages or lifestages, for which the evidence documented a role for Pb exposures (2011 REA Planning Document, Table 2-3). Similarly, in planning for the current review, we consider the current evidence (including data and models) and associated limitations and uncertainties with regard to quantitative analyses for effects other than IQ decrements in children (Table 2-4). The areas considered here include: (a) nervous system outcomes in children other than IQ decrements, (b) health outcomes in children other than neurobehavioral outcomes, (c) cardiovascular outcomes in adults and (d) health outcomes in adults other than cardiovascular outcomes.

The potential for development of quantitative exposure/risk analyses in these areas is considered in light of the information now available, e.g., with regard to the degree to which newly available data and information would support development of quantitative exposure/risk estimates (summarized in Table 2-4). As outlined in Table 2-4, the available evidence does not support estimation with confidence of exposures and risks for the outcomes and age groups listed above that can inform Pb NAAQS decision making. Key considerations in these evaluations are summarized here.

With regard to Pb-attributable endpoints for children other than IQ decrements, as summarized in Table 2-4, a number of factors affect our ability to quantify risks of these effects for Pb exposures of interest. For endpoints involving exposure extending to an age older than seven years, e.g., into the teenage years, we note the much greater uncertainty associated with predicting blood Pb in teenagers relative to younger, preschool-age children due to the greater complexity of both the timing and nature of Pb exposures during those years. Further, the studies supporting conclusions regarding cognitive endpoints other than IQ, specifically academic performance measures, rely on assessment metrics specific to a particular location (e.g., decrements in the passing rate for proficiency tests in a particular school system) challenging our ability to estimate risk relevant to the broader population of children in the United States (because exams are typically specific to each state, data cannot be directly compared across

states – draft ISA, Appendix 3, p.3-69). Similarly, other endpoints may involve particular at-risk populations (e.g., children born to mothers with increased rates of alcohol or drug use or children with coexposure to Pb and other metals) which again can impact the generalizability of risk estimates generated beyond the particular study population involved. As a whole, we find the information in support of risk estimates for IQ to remain the most robust among the endpoints for children, and such estimates have historically provided a strong foundation for NAAQS decision-making.

Regarding the development of quantitative risk estimates for health endpoints for adults, appreciable uncertainties in the evidence base affect our ability to reliably model those endpoints. While the evidence is sufficient to conclude that Pb exposure is causally related to several categories of effects in adults, including cardiovascular mortality, as in the last review, uncertainty remains with regard to the frequency, duration and magnitude of Pb exposures associated with these adult outcomes (draft ISA, Appendix 4, sections 4.10.1 and 4.10.2). In addition to these uncertainties, we note that the Pb exposure histories of the adult study populations in the epidemiology studies involve substantially higher Pb exposures, particularly during their childhood years due to the contemporary use of Pb in gasoline, than young adults of recent times, as is illustrated by the estimates of cumulative exposures in section 1.3.2.2 above. Accordingly, it is not currently possible to disentangle the influence of the substantial early and prolonged Pb exposures from the influence that much lower lifetime Pb exposure might exert on the associations observed in the available epidemiologic evidence between adult blood Pb and these health outcomes. Thus, the evidence does not support quantitative predictions of risk for adult health outcomes.

Table 2-4. Assessment of information (including methods and models) newly available in this review related to quantitative assessment of Pb endpoints other than IQ decrements in children.

Newly Available Information and Consideration of Potential Utility and Impact on Quantitative Exposure/Risk Assessment by Modeling Dimension
A) Neurobehavioral endpoints in children other than IQ In the 2008 review, while the 2006 AQCD described the evidence for a range of cognitive effects including deficits in academic achievement, effects in attention and executive function, behavioral effects and delinquent behavior, the REA focused on decrements in IQ for younger children due to the strength of the evidence for association with blood Pb levels below 10 μg/dL, and the strength of the dose-response information at these exposure levels (2007 REA, section 2.1.5). The REA Planning Document for the last review additionally concluded that the studies available at that time did not support quantitative risk assessment for neurodevelopmental endpoints besides IQ (2011 REA Planning Document, p. 2-32 and Table 2-3). The draft ISA identified five nervous system outcomes in children as being causally or likely causally associated with Pb exposure (draft ISA, Table IS-1). These include effects on cognitive function (including IQ), externalizing behaviors (attention, impulsivity and hyperactivity), internalizing behaviors (depression and anxiety), conduct disorders and motor function. In determining whether the scope of the REA should be expanded to incorporate additional endpoints in any of these outcome categories, we first consider the evidence with regard to the extent of the available information that might support estimating risk for the endpoints associated with Pb exposures of interest, and the associated limitations and uncertainties. We then consider the degree to which they could substantially enhance the assessment of the potential public health impact related to Pb exposure beyond that afforded by the current focus on IQ effects in younger children. In making this determination, we contrast overall uncertainty and other limitations associated with modeling risk for these endpoints with a similar calculus for the modeling of Pb-associated IQ effects in younger children. Careful consideration of the evidence available as a basis for modeling risk for endpoints in the above outcome categories results in a conclusion that the REA would not be significantly enhanced by expanding the scope to incorporate any of the above nervous system endpoints. Examples of the sources of uncertainty and limitations leading us to this conclusion regarding such expansion of the REA scope are presented below. With regard to cognitive function endpoints other than IQ, several epidemiology studies involved populations and/or endpoint metrics not readily generalizable outside of the specific context of the study, thereby limiting the degree to which risks based on those studies could be interpreted in the broader public health context for U.S. children. Specifically, a number of studies focus on standardized test performance (Evens et al., 2015, Blackowicz et al., 2016, and Shadbegian et al., 2019). However, as noted in Draft Pb ISA Appendix 3, section 3.5.1.6.4, because exams are typically specific to each state, data cannot be directly compared across states. This would make the generalizability of risk estimates associated with academic performance endpoints in the national-context more challenging. . Furthermore, limitations of each of these three studies would introduce uncertainty into risk estimates based on these studies' analyses. These limitations include (a) use of surrogates rather than direct measures for HOME inventory and parental IQ, both identified as strong confounders for blood Pb exposure (Evens et al., 2015, Blackowicz et al., 2016) and (b) failure to collect data on parental occupation and household income, both of which are determinants of academic performance for children (Shadbegian et al., 2019). A number of the studies across these outcome categories would require modeling of Pb exposures from birth through the teenage years resulting in blood Pb levels for older children (teenagers). Such estimation is associated with increased uncertainty compared to modeling blood Pb levels in younger children (0-7 years of age). This increased uncertainty results from the greater complexity in the pattern of Pb exposure for older children and the increasing role played by endogenous Pb in influencing changes in blood Pb which is a critical element of modeling changes in Pb exposure and hence risk. Most of the studies associated with academic performance, externalizing and internalizing behaviors fall into this category since they typically involve older children.

Newly Available Information and Consideration of Potential Utility and Impact on Quantitative Exposure/Risk Assessment by Modeling Dimension
A number of the studies also present challenges in terms of specifying C-R functions that might be appropriate for risk modeling. For example, studies investigating associations of effects on executive function with Pb exposures (e.g., Ruebner et al., 2019; Fruh et al., 2019; Braun et al., 2018) display a number of design elements that would pose obstacles to extracting a C-R function that could be used in predictive risk assessment. These include a focus on relating health outcomes to changes in dust Pb (but not to changes in total Pb exposure or in blood Pb levels), a focus on relating outcomes to maternal blood Pb (rather than child blood Pb), or a focus on specific subpopulations (e.g., children with chronic kidney disease). Similarly, regarding internalized behavioral endpoints (depression and anxiety), we note that some studies (e.g., Fruh et al., 2019) investigated health outcome associations with maternal (rather than childhood) exposure or blood Pb levels which complicates the specification and application of a C-R function. Additionally, a number of the studies involve child cohorts from earlier periods when blood Pb levels were elevated relative to today which reduces the representativeness of C-R functions based on these studies for our purpose of estimating risk for today's relatively lower Pb exposures. For example, in the context of impulsivity, a more recent study while focusing on younger children (Winter and Sampson, 2017) involves a group recruited while blood Pb levels were appreciably higher than they are today. Specifically, the cohort is from the late 1990s to early 2000s, with mean blood Pb level of 6.14 µg/dL, roughly three times higher than the 95th percentile for young children (1-5 yrs) in the 2017-18 NHANES (and ten times the mean), contributing uncertainty to consideration in the context of risk for today's children with relatively lower blood Pb levels. We also note the potential for greater subjectivity and hence bias in utilizing parent-measured metrics for some of the studies examining effects of Pb exposure on externalizing behaviors (e.g., ADHD). This is in contrast with more formally administered tests (e.g., of IQ) which would accordingly be expected to have reduced bias in the measurement of endpoint decrements. More recent studies focusing on ADHD have attempted to address these limitations, in particular Ji et al., 2018 (Draft Pb ISA, Appendix 3, section 3.5.2.7). Other limitations of the study by Ji et al. (2018) would introduce uncertainty into risk estimates generated based on that study's analyses. In particular, while the study adjusted for multiple major risk factors for ADHD identified in previous studies, the authors acknowledge that data related to multiple family-related factors such as poor parenting, maltreatment, conflict/parent-child hostility, and severe early deprivation were not available for the study cohort which introduces the potential for confounding. As with studies of externalized behavioral effects, we note that a number of studies examining internalized behavioral effects (anxiety and/or depression) involved non-US populations (e.g., Liu et al., 2014; Joo et al., 2018; and Horton et al., 2018) and while these studies may be relevant in assessing overall causality, they are not as relevant in deriving C-R functions for use in modeling risk to characterize public health impacts in the U.S.
B) Other health endpoints in children (beyond those for nervous system) In the 2008 review, the 2006 AQCD described the evidence for health outcomes in children other than nervous system effects, including hematological and immune effects, the strongest evidence for generating quantitative risk estimates was for neurodevelopmental effects and specifically, IQ decrements. In the current review, in addition to nervous system effects, the draft ISA identified several health outcome categories, including cardiovascular, renal, hematological and immunological, developmental and reproductive effects as being causally or likely causally related with Pb exposure (draft ISA, Table IS-1). Many of the challenges identified above for quantitative risk analyses of Pb effects on nervous system endpoints besides IQ (e.g., challenges in modeling Pb levels for older children, challenges in specifying C-R functions) also apply to other categories of health endpoints. Together these challenges affect the suitability of studies focused on other health outcomes for quantitative assessment in the context of this review. Furthermore, given the status of IQ in children as an endpoint with clear public health significance and with epidemiologic data that supports derivation of C-R functions, the increased value in attempting to model non-neurological endpoints in children with their increased uncertainty is not clear.

Newly Available Information and Consideration of Potential Utility and Impact on Quantitative Exposure/Risk Assessment by Modeling Dimension
C) Cardiovascular-related health endpoints in adults As discussed in the draft ISA, the evidence supports a causal relationship between cardiovascular effects, including cardiovascular mortality, and Pb exposure (draft ISA, Appendix 4, section 4.12). In planning for the 2016 NAAQS review, we considered the extent of support in the evidence for quantitative risk analyses for cardiovascular endpoints. In so doing, we noted the substantial uncertainty associated with the interpretation of the exposures eliciting the effects analyzed in adult epidemiology studies due to the extensive historical exposures experienced by the study cohorts, which influenced the study cohort blood and bone Pb measurements, and the cohort susceptibility. Additionally, at that time, ongoing research had not substantially reduced uncertainty related to predicting changes in blood Pb or bone Pb associated with reductions in ambient air Pb related exposures (2011 REA Planning Document, Table 2-3). Such uncertainties remain in the current review. As described in the draft ISA, adult blood Pb levels may be representative of contributions from both recent Pb exposures and mobilization of legacy Pb from bone (draft ISA, Appendix 2, section 2.3.5.2). Additionally, the risk of cardiovascular health effects may be influenced by biological responses to the elevated, earlier-in-life exposures. Accordingly, it remains unclear to what extent either recent, past, or cumulative Pb exposures contribute to the observed associations with cardiovascular mortality (draft ISA, section 4.10.2). Due to the appreciably greater ambient air Pb concentrations and population blood Pb levels prior to the phase out of leaded gasoline, the larger majority of study populations in the epidemiologic studies of Pb and cardiovascular mortality (and all of the older individuals) would be expected to have had significantly elevated blood Pb levels during earlier stages of their lives than the time of the blood Pb measurements analyzed in the epidemiologic studies, further complicating the determination of blood lead levels that might contribute to the observed associations reported in these studies (see Table 1-3 in section 1.3.2.2 and draft ISA, Appendix 4, section 4.10.1). A number of studies of cardiovascular health endpoints have employed NHANES study populations to assess the association of the outcomes with Pb exposure. These studies (and their NHANES study population and follow-up period) include: Cook et al. (2022), NHANES 1988-1994, 18 yr follow up; Menke et al. (2006), NHANES III 1988-1994, 13 yrs; Akoi et al. (2016), NHANES 1999-2010, 13 yr; Ruiz-Hernandez et al., (2017), NHANES III, 1988-1994 NHANES 1999-2004, 8-9 yrs; Lanphear et al. (2018), NHANES III 1988-1994, 24 yrs. Consideration of the blood Pb levels recorded across the NHANES samples indicates the appreciable lifetime exposures experienced by the majority of these cohorts, and the extent to which they are greater than those of today's young adults. For example, as illustrated by the cumulative Pb exposure estimates for different cohorts summarized in section 1.3.2.2 above, cohorts born in 1945 or 1970 would reasonably be estimated to experience, by age 50, as much as five to ten times the Pb exposures of a cohort born in 1990. Even the cohort born in 1990 would, by age 50, be reasonably estimated to experience twice the Pb exposure of a cohort born in 2010 (section 1.3.2.2 above). Data from NHANES indicates that the older individuals (e.g., older than 50 years) included in the cardiovascular mortality studies who might be expected to comprise the majority of the cardiovascular-related deaths analyzed, and who spent a significant portion of their earlier life during the period of elevated Pb exposure in the U.S., had quite high blood Pb levels in their younger years. For the most recent NHANES cohort studied (1999-2010 in Akoi et al. [2016]), the older individuals (>50 yrs of age) would have been at least ~20 to 25 years old in 1980, after having experienced a full childhood during the substantially elevated Pb exposure period of leaded gasoline. Similarly, regarding the study by Duan et al. (2020) that evaluated associations of cardiovascular mortality and blood Pb for NHANES participants enrolled in cycles between 1999 and 2014, the draft ISA notes that "[a]lthough some members of this population may have had lower Pb exposures due to the phaseout of leaded gasoline, especially when compared with studies assessing adults in NHANES II (1976–1980) and NHANES III (1988–1994), the vast majority of the participants were born well before the phaseout" (draft ISA, Appendix 4, p. 4-78). This observation is even more pronounced for studies of earlier NHANES populations, who would have spent substantially larger fractions of their earlier lives during the U.S. period of appreciably elevated Pb exposure. While the epidemiologic evidence of a statistical association between blood Pb and cardiovascular effects including mortality is supported by toxicological evidence, leading to the ISA conclusion of a causal relationship of cardiovascular effects (including mortality) with Pb exposure, challenges in identifying the

Newly Available Information and Consideration of Potential Utility and Impact on Quantitative Exposure/Risk Assessment by Modeling Dimension
specific nature and pattern of Pb exposures that elicit these cardiovascular effects introduces substantial uncertainty into predictive risk estimation for a simulated population without such appreciable exposure histories. Although, recent NHANES-based analyses that evaluate cardiovascular mortality associations with more recent adult blood Pb levels continue to observe strong associations, "these analyses still contain populations greatly influenced by high historic Pb exposure" (draft ISA, Appendix 4, section 4.10.2). As concluded in the draft ISA, "given the appreciable history of exposure in decades past (see Appendix 2, Section 2.4.1), and that Pb accumulates in the body over a lifetime, the extent to which past Pb exposures contribute to the BLLs and positive associations reported in epidemiologic studies remains uncertain" (draft ISA, Appendix 4, p. 4-76).
D) Health endpoints in adults other than cardiovascular effects The evidence supports causal or likely causal relationships for Pb exposure and several adult health outcomes other than cardiovascular outcomes. The limitations and uncertainties for cardiovascular outcomes, as discussed above, also pertain to these outcomes. More specifically, uncertainty in specifying the nature and pattern of Pb exposure that is eliciting the cardiovascular endpoints in cohorts with substantial Pb exposure histories also exists for other categories of adult health endpoints. In particular the reality of earlier periods of substantially higher Pb exposures for older-adult study populations complicates our understanding of the extent to which the associations observed in the studies are influenced by the earlier in life exposures, introducing significant uncertainty into any risk estimates generated for a simulated population without such significant exposure histories.

2.3 INITIAL PLANS FOR THE CURRENT REVIEW

In planning regarding a new exposure and health risk assessment for this review, we have considered how the exposure/risk information has supported judgments and decisions in the past two Pb NAAQS reviews, as well as the availability of new information that could reduce uncertainties, address limitations, and appreciably impact a revised or updated assessment. Together, these considerations contribute to our conclusions regarding the extent to which a new or substantially revised REA is warranted by the currently available information and, as warranted, the general scope and approach for such an assessment.

In considering the role of exposure/risk estimates drawn from the 2007 REA in informing decisions in the 2008 and 2016 NAAQS reviews, we note the associated key limitations and uncertainties of the estimates broadly as well as increased uncertainties for estimates from some specific case studies. While the Administrator gave primary consideration to estimates based on an evidence-based framework in the 2008 review, the risk estimates provided a perspective on the potential magnitude of air-related IQ decrements associated with the then-current standard in support of the conclusion that the then-current standard did not provide the requisite protection of public health (73 FR 66987, November 12, 2008). Given associated limitations and uncertainties, the risk estimates were somewhat less informative to identifying a specific revised standard. Rather, the risk estimates provided support to the evidence-based framework which guided the Administrator's decision on a specific level for the revised standard (73 FR 67006, November 12, 2008). In considering the risk estimates as to support for estimates based on the evidence-based framework, the EPA placed greater emphasis on estimates for the generalized local case study and the primary Pb smelter subarea case study, the two case studies that represent population exposures for more highly air-pathway exposed children residing in small neighborhoods or localized residential areas with air concentrations nearer the standard level being evaluated (a construct most comparable to that of the evidence based framework). By contrast, estimates from the location-specific (urban) case studies were for populations having a broader range of air related exposures including many with air-related Pb exposures well below the standard level being evaluated. Although these case studies provide risk estimates representative of populations in urban areas more broadly, they are less relevant to the single exposure zone construct of the evidence-based framework.

In the 2016 review of the Pb NAAQS established in 2008, EPA focused on both the risk estimates generated for the generalized local case study (then called the general urban case study), due to its simplified design and more direct comparability to the evidence-based framework, and the location-specific case study for Chicago due to the similarity of the current conditions scenario for that case study to expectations for air quality associated with the current

standard (81 FR 71925, October 18, 2016). Our planning regarding a new exposure/risk assessment in the current review has been informed by these past judgments regarding limitations, uncertainties and designs of the 2007 case studies.

Based on (a) the potential for addressing key limitations and uncertainties in the 2007 REA using new information/data (see section 2.2.1 above) and (b) the role played by the 2007 REA in informing the 2008 and 2016 NAAQS reviews (summarized immediately above), we have identified key considerations for preliminary planning with regard to conducting an REA as part of the current Pb NAAQS review. The analytical approach being considered for the current REA, which reflects integration of the elements detailed in the bullets below, is presented in Figure 2-5. We emphasize that the approach outlined here is subject to ongoing modification and refinement as we continue to consider new data/information (including the evaluation of that information in development of the ISA for this review) and consider comments provided by the public and CASAC in response to this document. Key elements of an analytical approach for a REA that might inform the current review include:

- *Health endpoint, age cohort and pathway apportionment:* The current information supports a continued focus on modeling risk of IQ decrements for young children exposed from birth up to seven years of age. As in the 2007 REA, we would expect to model total Pb exposure and risk, with pathway apportionment allowing us to apportion the estimates to 'recent air' and 'recent plus past air' pathways (with this pair of estimates providing the bounding estimates for ambient air Pb-related exposure and risk). We may consider modeling ADHD (change in probability of child developing ADHD as a result in change in Pb exposure). However, given limitations in the available study data supporting modeling of this endpoint (see Table 2-4), this endpoint would be included as a sensitivity analysis.
- *IEUBK blood Pb modeling and application of the GSD:* As in 2007, we expect to model central tendency exposures using IEUBK and pathway-specific Pb intakes to generate central-tendency blood Pb estimates to which an updated GSD(s) would be applied to characterize the variability (due to exposure-related behavioral and biokinetic factors, see section 2.1.1 above) in blood Pb levels for the study population.
- *Case study selection*: We would expect to include a case study similar to the generalized local case study. This simplified construct provides exposure and risk estimates for a single very near-source exposure zone, rather than estimates across the gradients common for air-related Pb that would be based on a detailed spatial analysis of exposure. While this approach provides estimates for what is expected to be an extremely small portion of population (children living immediately near sources where the standard is just met), it may be sufficient to provide insight on the adequacy of the current standard. Depending on findings for this case study, it may be appropriate to consider other case studies providing a broader representation of population exposure and risk. As discussed in Table 2-3 above, the limited spatial coverage of air Pb monitors is a source of uncertainty to estimates of spatial gradients

in air Pb concentrations in urban areas, as was recognized for the location specific (city-level) case studies completed for the 2007 REA.

- *Use of an updated hybrid indoor dust Pb model:* New information is available to support updates to the hybrid indoor dust Pb model, particularly the loading-to-concentration conversion step and AER data (as summarized in Table 2-3). Consideration for the prevalence of hardwood versus carpeted flooring can also affect the buildup of indoor dust Pb since flooring type can impact cleaning efficiency. Given non-linearities associated with the hybrid model (as noted in the 2007 REA) and the role of this model in linking ambient air Pb to indoor dust Pb (a critical air-related exposure pathway), refinements/updates to this model may have substantial impacts on the modeling of exposure and risk.
- *Specifying the C-R function for estimating Pb-associated IQ decrements in children:* To reduce the extent of extrapolation beyond the blood Pb levels on which the C-R functions are based, we would intend to utilize functions derived for the subset of study populations in the Lanphear et al. (2005) and Lanphear et al. (2019) pooled dataset that comprised the majority of the low-exposure observations, which included the Boston and Rochester cohorts. In applying these C-R functions, the resulting risk estimates will be characterized with regard to the extent to which they involve extrapolation beyond the range of the observations on which the C-R functions are based, with attention to the increased uncertainty associated with that extrapolation.
- *Characterization of uncertainty:* A range of sensitivity analyses may be considered for important elements of the REA including potentially: (a) the factors converting from the form of the standard to an annual average ambient air Pb level, (b) parameterization of the hybrid indoor dust Pb model, (c) GSD representing variability in blood Pb around a predicted central tendency value, and (d) C-R function for IQ decrement. In addition to these sensitivity analyses, we also will recognize uncertainty associated with exposure/risk estimates based on ranges of exposure beyond those supported by the overall REA model. Identification of such exposure ranges will likely include consideration of the performance ranges evaluated for the three main components of the REA (hybrid indoor dust model, IEUBK blood Pb modeling including application of the GSD and the C-R functions for IQ decrement). Each of these has an associated range of exposure for which the component has been validated (hybrid dust model and IEUBK) or which is reflected in the underlying observational data (interindividual variability GSD, C-R function). To the extent instances where exposure and risk estimates fall outside of one or more of these modeling component ranges can be identified, associated reduction in overall confidence for those exposure/risk estimates will be noted. Such an assessment of confidence related to application of the three components of the REA model may be informative to interpretation of exposure/risk estimates for the current standard and, as applicable, any alternatives that may be considered. In addition, as with previous NAAQS-related REAs, we will complete a characterization of uncertainty utilizing the WHO framework (WHO, 2008). The WHO's four-tiered approach matches the sophistication of the assessment of uncertainty to the overall complexity of the risk assessment, while also considering the potential magnitude of the impact that the risk assessment can have from a regulatory/policy perspective (e.g., risk assessments that

are complex and are associated with significant regulatory initiatives would likely be subjected to more sophisticated uncertainty analysis). The WHO framework includes the use of sensitivity analysis both to characterize the potential impact of sources of uncertainty on risk estimates and to generate an array of reasonable risk estimates.

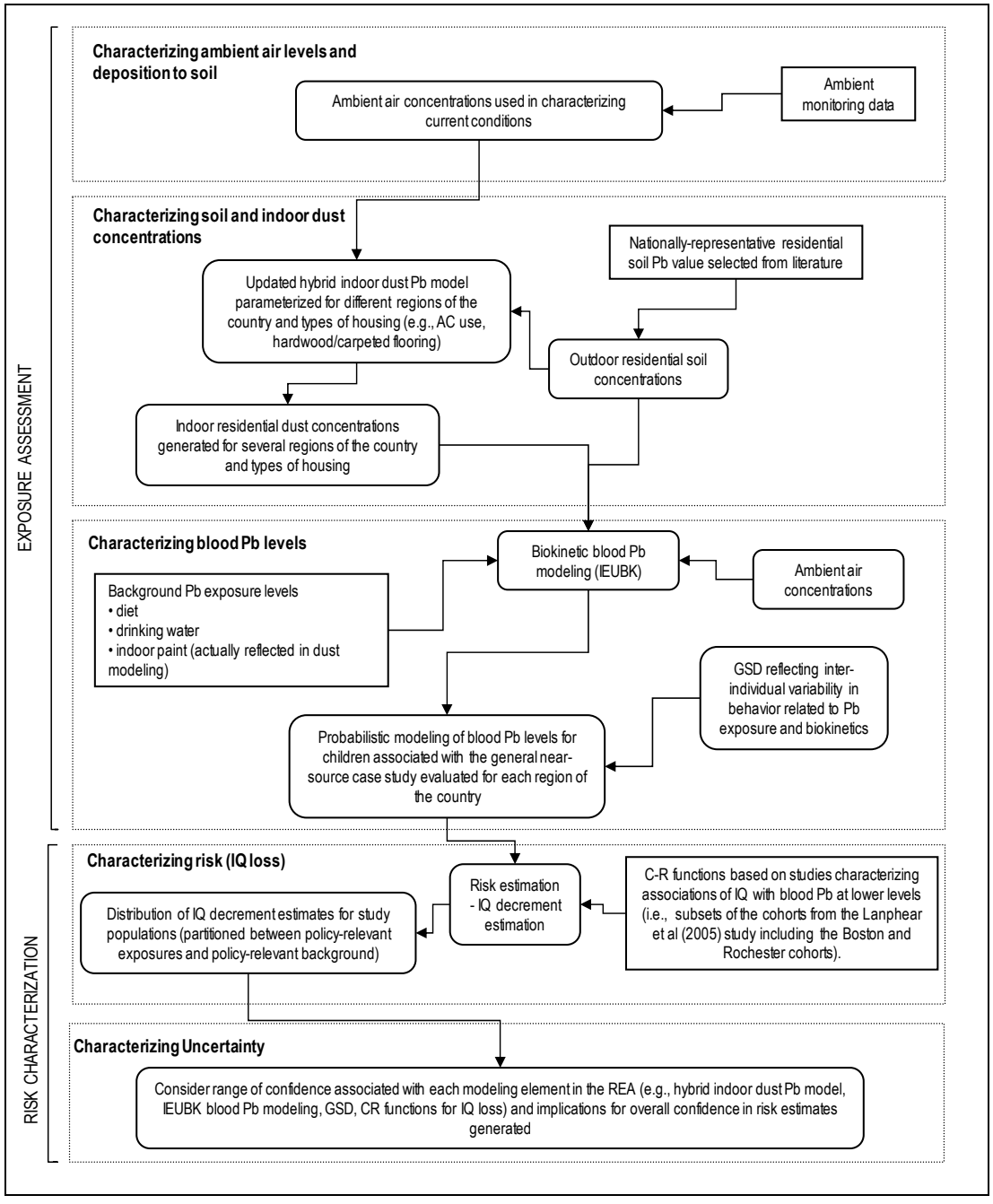

Figure 2-5. Analytical approach for the REA under consideration for the current review.

3 QUANTITATIVE ANALYSIS PLANNING FOR THE SECONDARY STANDARD

In reviews of secondary NAAQS, quantitative exposure/risk analyses are generally intended to assess ecosystem exposure and welfare risk for air quality conditions associated with the existing standards and, as appropriate, for conditions associated with potential alternative standards. The objective for such assessments is then to provide quantitative estimates of impacts that inform judgments on the public welfare significance of exposures likely to occur under air quality conditions reflective of the current NAAQS and, as appropriate, any alternative standards under consideration. Accordingly, the assessments are also intended to provide a basis for judgments as to the extent of ecological welfare protection afforded by such standards. Thus, the assessments are generally intended to inform consideration of key policy relevant questions (*See* IRP, volume 2), such as the following:

- What are the nature and magnitude of exposures and ecological/welfare risks associated with air quality conditions just meeting the current standard?
- To what extent are the estimates of exposures and ecological risks associated with air quality conditions just meeting the current standard reasonably judged important from a public welfare perspective?

In considering exposure/risk estimates in this context, an accompanying consideration is:

- What are the important limitations and uncertainties associated with any risk/exposure estimates?

In this planning document, our evaluation of information available in this review is intended to inform judgments regarding the extent to which the available information supports development of a new quantitative risk assessment likely to contribute to substantively new conclusions regarding the risk to welfare associated with Pb in the ambient air to inform the Administrator's judgment of the adequacy of protection against adverse environmental effects afforded by the current NAAQS. This evaluation is structured around consideration of two key questions:

- Is there newly available information relevant to critical uncertainties or limitations associated with the ecological risk information in the last review?
- To what extent does the currently available information support the development of an updated or new quantitative risk assessment that would generate results providing more specific or more certain estimates of ecological risk associated with the current Pb secondary standard?

In designing and implementing an assessment of exposure and risk associated with Pb, we face a level of complexity substantially greater than for similar assessments typically

performed for other criteria pollutants. Unlike most other pollutants for which NAAQS are established, Pb is a multimedia and persistent pollutant. Risk associated with exposure to Pb originally released to ambient air is multimedia in nature, with exposure and risk associated with a range of pathways associated with deposition of ambient air Pb. Exposure of terrestrial animals and vegetation to air-related Pb can occur by contact with ambient air or by contact with soil, water or food items that have been contaminated by Pb from ambient air (ISA, section 6.2). Transport of Pb into aquatic systems similarly provides for exposure of biota in those systems, and exposures may vary among systems as a result of differences in sources and levels of contamination, as well as characteristics of the systems themselves. Further, the persistent nature of Pb means that exposure and risk can be associated with Pb originally emitted into the ambient air recently or at some point in the past, from current or historic sources, under conditions associated with previous Pb NAAQS or prior to the existence of any Pb NAAQS. Such historically emitted Pb can also then be transported through other media (e.g., contributing to Pb in a water body via runoff from soils near historical air sources). Additionally, ecological exposures and risk also result from uses of Pb that contribute Pb to the environment without it passing through ambient air, such as land and water disposal of wastes, weathering of structures with lead-based paint, leaching of solder used in water distribution systems into water that flows through wastewater treatment facilities and land uses such as mining.

In considering the extent to which the currently available information warrants development of updated quantitative exposure/ risk assessments in this review – and, as warranted, in considering approaches and design aspects for any such assessments – we will assess both the availability of new air quality data and data or estimates for other media that might inform consideration of the current Pb standard, as well as any newly available scientific evidence that indicates a more refined understanding of the effects of deposited ambient air Pb on ecosystems and organisms. More specifically, we focus on 1) the ability of current data sets and tools to characterize exposure of ecosystems to ambient air Pb deposited in association with air quality meeting the existing standard and 2) the availability of new evidence that would allow the current review to develop more robust assessments of associated welfare risk than available in the last review.

3.1 CONSIDERATION OF 2006 ASSESSMENT IN PRIOR REVIEWS

The 2011 REA Planning Document (for the 2016 review) described our consideration of the assessment conducted in 2006 to inform the 2008 review, and particularly the extent to which its limitations and uncertainties could be addressed by information newly available at that time. The conclusion, with which the CASAC Pb Review Panel in that review generally concurred, was that the information available since the preceding (2008) review, with regard to designing

and implementing a full REA that would appreciably address limitations and uncertainties of the prior assessment, was such that performance of a new REA was not warranted. Accordingly, the risk assessment information available for consideration in the 2016 review was based on the screening-level risk assessment which informed decisions in the prior, 2008, review ((U.S. EPA, 2006b [referred to as the 2006 REA]; 2007 Staff Paper; 73 FR 66964, November 12, 2008).

The 2006 assessment focused on estimating the potential for ecological risks associated with ecosystem exposures to Pb emitted into ambient air (2014 PA), section 5.2; 2006 REA, section 7). Both a national-scale screen and a case study approach were used to evaluate the potential for ecological impacts that might be associated with atmospheric deposition of Pb (2014 PA, section 5.2; 2006 REA, section 7.1.2).[18] The risk information from the 2006 REA analyses informed to varying extents, and with associated limitations, the risk-based considerations in the 2008 review regarding the potential for adverse welfare effects to result from levels of air-related Pb that would meet the existing standard at that time.

The national-scale screen in the 2006 REA evaluated surface water and sediment monitoring locations across the U.S. for the potential for ecological impacts that might be associated with atmospheric deposition of Pb (2006 REA, section 7.1.2). In addition to the national-scale screen (2006 REA, section 3.6), the assessment involved a case study approach, with case studies for areas surrounding a primary Pb smelter (2006 REA, section 3.1) and a secondary Pb smelter (2006 REA, section 3.2), as well as a location near a non-urban roadway (2006 REA, section 3.4). An additional case study focused on consideration of atmospherically derived Pb effects on an ecologically vulnerable ecosystem, the Hubbard Brook Experimental Forest (HBEF), in the White Mountain National Forest near North Woodstock, New Hampshire (2006 REA, section 3.5). The HBEF case study was a qualitative analysis focusing on a summary review of the literature, without new quantitative analyses (2006 REA, Appendix E).[19] For the other three case studies, exposure concentrations of Pb in soil, surface water, and/or sediment were estimated from available monitoring data or modeling analysis and then compared to ecological screening benchmarks (2006 REA, section 7.1). In the discussion below, we summarize these various components of the 2006 assessment, with a focus on limitations and associated uncertainties in interpretation of their findings (see also Table 3-1).

[18] Detailed descriptions of the location-specific case studies and the national screening assessment, key findings of the risk assessment for each, and an interpretation of the results with regard to past air quality conditions are presented in the 2006 REA, summarized in section 5.2 of the 2014 PA and in section III.C of the 2015 proposal (80 FR 317-319, January 5, 2015).

[19] The HBEF was selected as a case study because of its location and its extensive data record on trends of Pb concentrations in three media (air or deposition from air, soil, and surface water).

In the 2006 screening assessment, the non-air media exposure estimates for the first three case studies, and the national-scale screen for surface water and sediment, indicated a potential for adverse effects from environmental Pb to multiple ecological receptor groups in terrestrial and aquatic locations. However, the extent to which non-air sources or past air emissions of Pb, under air quality conditions that did not meet the existing standard, had contributed to the surface water or sediment Pb concentrations assessed is unclear.

- For example, at some of the locations in the national-scale surface water and sediment screen, non-air sources likely contributed significantly to the surface water Pb concentrations. For other locations, a lack of nearby non-air sources indicated a potential role for air sources to contribute to observed surface water Pb concentrations. However, these concentrations may have been influenced by Pb in resuspended sediments and may reflect contribution of Pb from erosion of soils with Pb derived from historic as well as current air emissions. Given the appreciable changes in ambient air Pb concentrations prior to the 2016 review, these uncertainties limited the extent to which these national screens were informative to the 2016 consideration of the existing standard. Given the more restrictive standard being reviewed in 2016 (than that in 2008), this limitation loomed larger in 2016 than in the 2008 review of the standard set in 1978. With regard to the case studies, the specific circumstances of the point source and near-roadway case studies also contributed uncertainty which limited conclusions with regard to ambient air Pb concentrations of interest.
- For the primary Pb smelter case study, while the contribution to Pb concentrations from air, as compared to non-air sources, is not quantified, air emissions from the smelter facility were substantial (2006 REA, Appendix B). In addition, this facility, which closed in 2013, had been emitting Pb for many decades, including some seven decades prior to establishment of any Pb NAAQS, such that it is likely air concentrations associated with the facility were substantial relative to the 1978 NAAQS, which it exceeded at the time of the last review. At the time of the 2016 review and also since the adoption of the current standard, concentrations monitored near this facility have exceeded the level of the applicable NAAQS (2007 Staff Paper, Appendix 2B-1; 2014 PA, Appendices 2D and 5A). Accordingly, the 2016 conclusion regarding this case study was that it was not informative for considering the likelihood of adverse welfare effects related to Pb from air sources under air quality conditions associated with meeting the existing Pb standard.
- At the time of the 2016 review, the secondary Pb smelter case study location continued to emit Pb, and the county where this facility is located did not meet the current Pb standard (2014 PA, Appendices 2D and 5A). Given the exceedances of the current standard, which likely extend back over four to five decades, this case study was also concluded to not be informative for considering the likelihood of adverse welfare effects related to Pb from air sources under air quality conditions associated with meeting the existing Pb standard.
- As to the near-roadway non-urban case study, its locations were recognized to be highly impacted by past deposition of gasoline Pb. Given evidence from the past of Pb concentrations near highways that ranged above the previous (1978) Pb standard

(U.S., 1986 [1986 AQCD], section 7.2.1), it was concluded in the 2016 review that conditions at these locations during the time of leaded gasoline very likely exceeded the existing standard. Similarly, those conditions likely resulted in Pb deposition associated with leaded gasoline that exceeds that being deposited (or resuspended and redeposited[20]) under air quality conditions that would meet the existing Pb standard. Given this legacy, it was concluded that the potential for environmental risks from levels of air–related Pb associated with meeting the existing Pb standard in these locations is highly uncertain.

The most useful case study to the 2016 review was that of the Vulnerable Ecosystem Case Study located in the HBEF. This case study was focused on consideration of information which included a long record (from 1976 through 2000) of available data on concentration trends of Pb in three media (air, soil, and surface water) and on air deposition. While no quantitative analyses were performed, a summary review of literature published on HBEF was developed. This review indicated: (1) atmospheric Pb inputs do not directly affect stream Pb levels at HBEF because deposited Pb is almost entirely retained in the soil profile; and (2) soil horizon analysis results showed Pb to have become more concentrated at lower soil depths over time, with the soil serving as a Pb sink, appreciably reducing Pb in pore water as it moves through the soil layers to streams (dissolved Pb concentrations were reduced from 5 μg/L to about 5 ng/L from surface soil to streams). As a result, this case study, and the HBEF studies on which it was based, concluded that the contribution of dissolved Pb from soils to streams was insignificant (2006 REA, Appendix E). Further, atmospheric input of Pb, based on bulk precipitation data, was estimated to decline substantially from the mid-1970s to 1989; forest floor soil Pb concentrations between 1976 and 2000 were also estimated to decline appreciably (2006 REA, sections E.1 and E.2). In considering HBEF and other terrestrial sites with Pb burdens derived primarily from long-range atmospheric transport, the 2006 AQCD found that "[d]espite years of elevated atmospheric Pb inputs and elevated concentrations in soils, there is little evidence that sites affected primarily by long-range Pb transport have experienced significant effects on ecosystem structure or function" (2006 AQCD, p. AX7-98). The explanation suggested by the 2006 AQCD for this finding is "[l]ow concentrations of Pb in soil solutions, the result of strong complexation of Pb by soil organic matter" (2006 AQCD, p. AZX7-98). While more recent soil or stream data on Pb concentrations were not available, it was considered unlikely in the 2016 review, given the general evidence for air Pb emissions and concentration declines over the past several decades (e.g., 2014 PA, Figures 2-1, 2-7 and 2-8), that conditions would have worsened from those on which these conclusions were drawn (e.g., soil data through 2000). Therefore, this information

[20] Air Pb concentration trends at a limited set of near-roadway monitors in the 2013 PA provides evidence of the decline in concentrations from the time of on-road leaded gasoline usage, and the current concentrations, at such sites (2014 PA, Figure 2-9).

was found to suggest that the lower ambient air concentrations associated with meeting the standard set in 2008 would not be expected to directly impact stream Pb levels.

In summary, the nationwide surface water screen was not particularly informative to evaluation of the adequacy of the 2016, or 2008, secondary Pb standard because potential confounding by both non-air inputs and resuspension of Pb related to historic sources was not easily accounted for. Further, the circumstances assessed in all but one of the case study locations likely include a history of ambient air Pb concentrations that exceeded the NAAQS set in 1978. For example, Pb deposited before that standard was enacted remains in soils and sediments, complicating interpretations regarding the impact of the current standard; historic Pb emitted from leaded gasoline usage continues to move slowly through systems along with more recently deposited Pb and Pb derived from non-air sources (2014 PA, section 1.3.2). Consequently, in the 2016 review, these analyses were not considered informative for predicting effects at the far lower concentrations associated with the current NAAQS.

Salient aspects and associated limitations and uncertainties of the national screen and case study approach employed in the 2006 REA (screening assessment) for the 2008 review are summarized, along with important limitations and uncertainties, in Table 3-1 below. As indicated above and in Table 3-1, a critical limitation of some of these analyses related to a lack of clarity with regard to contributions from sources other than atmospheric deposition. Uncertainty associated with that limitation is reduced for case studies, such as HBEF, for which non-air Pb sources are unlikely. While the HBEF case study proved informative to judgments regarding air contributions to non-air media, uncertainty remains with regard to quantitative characterization of the associated ambient air Pb concentrations.

Table 3-1. Limitations and uncertainties of the exposure/risk analyses for the 2008 review, and consideration of related newly available information. Drawn from the 2011 REA Planning Document, 2014 PA; 2015 and 2016 notices of proposed and final decisions; and draft ISA**.**

Analysis Element	Summary of National Screens and Case Studies in 2006 REA (Screening Assessment), including Salient Observations Focused on Recognized Limitations/Uncertainty	Newly Available Information for Current Review
Approach for characterizing non-air exposures and linkages to air concentrations		
National-surface water & sediment screen	The limited availability of locations for which recent Pb measurements were available, and uncertainty regarding potential for non-air sources to have contributed to non-air media concentrations, limited our ability to assess media concentrations, nationally, likely to be associated with recent atmospheric Pb conditions and those associated with existing standard. The largest uncertainties are associated with our ability to apportion concentrations between air and non-air sources, with additional limitations in our ability to quantitatively characterize associated air Pb concentrations.	The limitations identified for the national screen and case studies relate to the connection between air concentration and ecosystem exposures, which continues to be poorly characterized for Pb and to the lack of information on the contribution of atmospheric Pb to specific sites, such that the limitations in application of a national screen and these case studies remain.
Primary and secondary smelter case studies	Exposure concentrations in soil, surface water, and/or sediment were estimated for the three case studies from available monitoring data or modeling analysis (2006 REA, sections 3.1-3.3), however air quality conditions for the modeling analyses as well as the monitoring data were well in exceedance of the existing standard, and the historical records also indicated contributions from non-air sources. Exceedances of the existing standard in these locations, which likely extend back over 4 to 5 decades, mean that these case study datasets are not informative to considering the likelihood of adverse welfare effects related to Pb from air sources under air quality conditions meeting the current Pb standard.	
Near-roadway case studies	These case study locations near established highways for which soil Pb data are available, are highly impacted by past deposition of gasoline Pb, providing information potentially useful for the standard existing in the 2008 review, although with uncertainty in estimating the associated air Pb concentrations. Given evidence from the past of Pb concentrations near highways that ranged above the previous (1978) Pb standard (1986 CD, section 7.2.1), conditions at these locations during the time of leaded gasoline very likely exceeded the existing standard, limiting their usefulness for estimating soil Pb concentrations associated with the existing standard.	
Hubbard Brook Experimental Forest Case Study	As a strength, this case study included a remote location, making atmospheric deposition the most likely contributor to environmental Pb, and the was a long record of available data on concentration trends of Pb in three media: air or deposition from air, soil, and surface water (2006 REA, Appendix E)). However, limitations in the availability of air concentration data hindered quantitative characterization of Pb air quality conditions. While this case study provided stream, soil and pore water Pb concentrations likely largely associated with air deposition sources, and supported qualitative conclusions regarding a lack of impacts of atmospheric Pb on stream Pb, either through direct deposition or transport of deposited Pb from surface soils, and with regard to patterns of Pb across soil depths under air quality conditions that may have met the existing standard, quantitative analysis with regard to air Pb concentrations was not feasible.	There are no recent publications on Pb in the HBEF. The most recent Pb air concentration data for this area comes from a monitor in Camp Dodge (3-7pprox.. 35 miles away) covering the years 1995-2021.

Analysis Element	Summary of National Screens and Case Studies in 2006 REA (Screening Assessment), including Salient Observations Focused on Recognized Limitations/Uncertainty		Newly Available Information for Current Review
Approach for characterizing potential for ecological impacts			
National-surface water & sediment screen Primary and secondary smelter and near-roadway case studies Hubbard Brook Experimental Forest Case Study	Media concentrations were compared to ecological screening benchmarks (e.g. Ecological Soil Screening Levels (Eco-SSLs) and Ambient Water Quality Criteria (AWQC)), which did not accommodate a more rigorous or detailed consideration of bioavailability characteristics influential to Pb toxicity in these media.	With regard to the extent of lead-related effects in the natural environment, it remains difficult to assess the concentrations at which Pb elicits specific effects in terrestrial and aquatic ecosystems, due to the influence of other environmental variables on both Pb bioavailability and toxicity and also due to substantial species differences in Pb susceptibility.	There is some new evidence with regard to bioavailability and its role in influencing the potential for effects in the environment. (See draft ISA, Appendix 11, Sections 11.2, 11.3, and 11.4) There is little new information that would facilitate extrapolation of evidence on individual species, generally from laboratory-controlled exposure studies, to conclusions regarding adversity to populations or ecosystems within the natural environment. (See draft ISA, Appendix 11, Sections 11.2, 11.3, and 11.4)
Approach for characterizing risk for adverse effects associated with existing NAAQS			
	Consideration of the environmental risks and potential welfare effects associated with the current standard is complicated by the environmental burden associated with air Pb concentrations, predominantly in the past, that exceeded both the previously existing standard and the current standard. The largest uncertainties are identified to be associated with our ability to determine the potential risk/extent of lead-related effects in the natural environment and to apportion effects between air and non-air sources, and with the relationship between effects and environmental conditions associated with the standard Overall, these remain the major sources of uncertainty in our evaluation of effects and exposure evidence for Pb in ecosystems.		

3.2 CONSIDERATION OF THE AVAILABLE EVIDENCE IN THE CURRENT REVIEW

In planning for any new assessments or evaluations in this review, we consider limitations and uncertainties of the prior assessment so as to direct any new analyses toward reducing these to improve upon the usefulness of the exposure/risk information considered in this review. Accordingly, critical at this planning stage is consideration of the extent of newly available evidence that may address these limitations or uncertainties or otherwise augment or improve upon the assessment from the last review. Thus, as in any review, key considerations in planning for new analyses that may be appropriate in this review include:

- Identification of aspects of the prior assessment for which updates are available and feasible and that may reduce uncertainty or address limitations, thus improving appropriateness of the assessment for its purpose; and
- Availability of new information or tools that have potential to address key areas of uncertainty or to provide new approaches to inform our understanding of environmental exposures and associated risk associated with air quality under the current standard.

In considering the extent to which the information available in this review warrants the conduct of new exposure/risk analyses and, as warranted, in identifying the types of assessments or evaluations to be developed or updated in this review, we give particular attention to the assessment approaches for which limitations and uncertainties were fewer and accordingly which were found to be most informative in the last review. As discussed in section 3.1 above, the evaluation found to be most informative in the last review focused on a multimedia dataset for a setting for which the source of environmental Pb was considered to be primarily atmospheric Pb under air quality conditions considered likely to have met the existing standard (the HBEF case study). This dataset was considered most relevant to our focus of characterizing Pb ecosystem exposures likely to reflect predominantly atmospheric sources under air quality conditions that would meet the current standard.

There are several areas of limited information from the last review which we consider below with regard to the availability of new information described in the draft ISA in this review. Our focus in these sections is on the extent to which the now available information addresses key limitations in developing quantitative analyses that would substantively and quantitatively inform consideration of the adequacy of the current secondary standard. Further, we note that with regard to ecosystem services, the draft ISA concluded that "Although the ecosystem services literature has expanded since the 2013 ISA, there are few publications that specifically link an ecological effect attributed to Pb to a change in an ecosystem service" (draft ISA, Appendix 11, section 11.1.5).

Key aspects of the assessment developed for the 2008 review, aspects of which also informed the last review, are briefly summarized in Table 3-1 above. As summarized there, key limitations generally relate challenges in characterizing the role of atmospheric Pb in non-air media exposures and associated quantitative relationships. In the 2016 review, our understanding of the complexities in relating non-air media concentrations to air concentrations that might be associated with the existing standard was also further informed by aspects of the evidence available at that time (e.g., Table 3-2).

Table 3-2. Additional studies/surveys available since the 2008 review that may inform characterization of non-air exposures associated with air Pb concentrations.

Study Type	Summary of Information Available in the 2016 Review, including Salient Observations Focused on Recognized Limitations/Un Certainty	Information Newly Available in the Current Review
Deposition Studies	Surveys newly reported in the 2013 ISA indicate mid-twentieth century peak in U.S. Pb deposition, with declines documented in locations remote from industrial areas, with stationary sources, and in industrial areas since the 1970s-80s (2013 ISA, sections 2.3.1; 2006 AQCD, section 2.3.1; Jackson et al., 2004; Watmough and Dillon, 2007; Sabin and Schiff, 2008). Such surveys provided little if any information on associated air Pb concentrations.	No new studies identified in draft ISA.
Soil Surveys	Studies in more remote forested areas continue to indicate gradual migration of deposited Pb into mineral soils since the 70s/80s (e.g., Miller and Friedland, 1994; Zhang, 2003), without corresponding air Pb measurements. In locations nearer point sources, historically deposited Pb (during periods existing standard was not met) complicates estimates of soil Pb concentrations that might be expected under conditions meeting the current standard. Findings to date indicate that many of those systems less influenced by current point sources have and may still be responding to reduced Pb deposition rates associated with reduced atmospheric emissions of Pb, including those associated with the phase-out of leaded gasoline for on-road vehicles, while potential responses of soils near point sources and those involving historically deposited Pb near roadways are less well characterized, but might be expected to have longer time horizons (2014 PA).	Recently available national and regional surveys of soil Pb concentrations (draft ISA, Appendix 11 section 11.1.3 and Table 11-1), and also peat core study (draft ISA, Appendix 1, section 1.3.3.4). See details in Table 3-3
Terrestrial Biota Surveys	Limited measurements of Pb in some biota indicate reductions in biologically available Pb over the past 30 years or more in some remote locations, such as Pb in lichen in Mount Ranier and Sequoia/Kings Canyon National Parks (2013 ISA, section 2.6.6; Landers et al., 2008); and Pb in teeth of juvenile and adult moose in Isle Royale National Park in northern Michigan (2013 ISA, section 2.6.8; Vucetich et al., 2009). Moss Pb concentrations near a hauling road for a zinc and Pb mine mining increased over the decade subsequent to initiation of the mine, with uncertainty associated with relative contribution of atmospheric distributed Pb *versus* truck fallout. Across these surveys, a lack of linkages to air Pb concentrations across the relevant temporal period limits more precise consideration of associated air Pb concentrations.	Recently available studies of Pb in tree rings (draft ISA, Appendix 11, Section 11.2.2.2) may be useful in informing our understanding of air Pb and associated uptake in the trees, to the extent information is also available regarding air Pb concentrations. See details in Table 3-3
Surface Water Surveys	Surveys in the 2006 AQCD were the focus of the National Surface Water Screen in 2008 review (see above). Updated information was not available in 2016 review.	No new studies identified in draft ISA.

Study Type	Summary of Information Available in the 2016 Review, including Salient Observations Focused on Recognized Limitations/Un Certainty	Information Newly Available in the Current Review
Sediment Surveys	Several studies of cores or surface concentrations have observed increases in concentration in the mid-nineteenth century continuing thru mid-twentieth century and more recent declining Pb in sediments usually attributed to leaded gasoline phaseout and industrial emissions reductions of 1970s-1990s. Included in these surveys are more remote areas, including lakes in several western U.S. National Parks (2013 ISA, section 2.6.2; Landers et al., 2010). The declining pattern since the 1970s-80s was also reported for cores in areas closer to metropolitan areas, with uncertainty regarding relative contribution of changes in surface water discharges versus air deposition, although upstream sites may be more reflective of atmospheric Pb influences (2014 PA).	Recently available study of sediment cores in Adirondack Mountain lakes remote from non-air Pb sources may be useful in informing our understanding of air Pb and associated sediment concentrations, to the extent information is also available that might inform an understanding of linkages to air Pb concentrations. (draft ISA, Appendix 1, Section 1.3.3.3). See details in Table 3-4
Aquatic Biota Surveys	Shellfish monitoring across a recent 20-year period provides varying patterns of temporal trends and is limited by combined contribution of site-specific environmental releases as well as other ecosystem influences on Pb fate and transport (2013 ISA, section 2.6.7; Kimbrough et al., 2008).	Recently available studies of Pb in shellfish and crustacea, depending on potential influence of non-air sources such as surface water discharges, may be informative to conclusions regarding air Pb and associated aquatic biota exposures, to the extent information is also available to assess linkages to air Pb concentrations. (draft ISA, Appendix 11, Section 11.4.2). See details in Table 3-5

3.2.1 Linking Atmospheric Pb to Non-Air Media Concentrations

As summarized in section 3.1 above, a critical challenge in assessing exposure and risk to ecological receptors relates to characterization of concentrations in non-air media associated with air quality conditions of interest. Contributing to this challenge are the multimedia aspects of Pb and its environmental persistence, coupled with the complexity of its movement among and within ecosystem compartments, as well as the historical environmental legacy of air

concentrations well in excess of the current Pb standard and the often obscuring environmental legacy of Pb that has not passed through ambient air, as recognized at the top of this chapter.[21]

Although the concept of critical loads has been described in the literature in the context of considering potential for ecosystem impacts from atmospheric deposition of some pollutants, many such approaches, including the very few publications that relate to Pb, do not account for bioavailability within ecosystem compartments, fluxes within systems and other non-air contributions.[22] Such limitations were noted in the 2006 AQCD with regard to Pb and remained in the 2018 ISA (2013 ISA, section 7.2.6).[23] The draft ISA for the current review identifies no advances to address these limitations. Accordingly, as concluded in the last review, substantial limitations remain in the data needed to incorporate the necessary components (flux, bioavailability, speciation, and source) at ecosystem levels in a way that could support a large-scale application of a model that might inform evaluation of ecosystem Pb loading to inform the NAAQS review.

Given the complexity of the temporal aspects of the distribution of Pb from air to other media, and in light of the many past years of appreciably greater air concentrations than those allowed by the current NAAQS, in our consideration of the currently available evidence, we consider the potential usefulness of studies that characterize temporal trends in various environmental media. Trends observed in such studies and the extent to which they provide a basis for relating some characterization of non-air media concentrations to air Pb concentrations could prove informative to judgments concerning potential for impacts to the public welfare under air quality conditions allowed by the current standard. Currently available studies of this type available for consideration in this light are summarized in Tables 3-3 through 3-5 below.

[21] This includes Pb entering the environment from land and water disposal of wastes, weathering of structures with lead-based paint, leaching of solder used in water distribution systems into water that flows through wastewater treatment facilities and land uses such as mining.

[22] There also significant limitations on the information that might inform the Administrator's judgments on appropriate endpoints and targets on which to base identification of critical loads appropriate to inform decision-making on a secondary standard protective of the public welfare.

[23] The 2013 ISA noted that there were many uncertainties inherent in a critical load approach to Pb risk assessment, such as soil type, critical concentration of dissolved metals, and the absorption coefficients of exposed soils, and that despite a greater understanding of critical load modeling in other reviews (such as with regard to critical loads for acidic nitrogen and sulfur compounds in vulnerable freshwater systems), we are still strongly limited with regard to data to quantify these processes and influences adequately in such modeling of U.S. ecosystems for Pb. Since the 2013 ISA, no recently published loading analyses for Pb for terrestrial ecosystems or for atmospheric deposition of Pb to inland or coastal water in the U.S. have been identified (draft ISA, Section 11.1.7.1).

Table 3-3. Studies describing temporal trends in Pb in soil, peat and terrestrial biota

Study Description	Location/Time Period	Description of Temporal Trends	Notes
Regional survey of forest floor soils sampled in Northeastern US (PA, NY, NH, MA, VT, and CT) (Richardson et al. 2014; draft ISA, Appendix 1, section 1.3.2.3)	16 sites across deciduous and mixed deciduous/coniferous forests 1980-2011 with individual year sampling in 1980, 1990, 2002, and 2011.	Across all sites, mean soil Pb concentrations decreased from 151 ± 29 (SE) mg Pb/kg in 1980 to 68 ± 13 (SE) mg Pb/kg in 2011.	Isotopic analysis of Pb samples indicates gasoline Pb as the dominant source of soil Pb. Many study site locations are in rural areas which may have limited Pb input from media sources other than air deposition.
Dendrochronology study of spruce, beech, white pine, and cedar tree species in Eastern Canada (Doucet et al. 2012; draft ISA, Appendix 11, Section 11.2.2.2)	Reconstructed Pb trends from 1880-2007	Beech trees recorded decline in concentrations after a 1970-1985 peak.	Long-term Pb composition of pine and red spruce species was interpreted to be influenced by internal physiological mechanisms (radial mobility) and was not used to infer air pollution history of respective sites. Beech species seemed to exhibit less Pb radial mobility and were consistent with the paleolimnological profile. The authors suggest combining several tree species to study past air pollution history.[A]
Dendrochronology study of white spruce trees in Northern Athabasca Oil Sands of Western Canada (Dinis et al. 2016; draft ISA, Appendix 11, Section 11.2.2.2)	1878-2009	Relative Pb concentrations increased beginning in 1922, peaked in 1968-1973, then decreased until 2009.	
Samples of Pb in Lichen from Golden Lake in Mount Rainier National Park (2005) and Emerald Lake Basin in Sequoia/Kings National Parks (2004) (Landers et al. 2008; 2013 ISA, Section 2.6.6)	Initial sampling in 1984 at both MRNP and Sequoia/Kings NP, then resampled in 2005 and 2004 respectively.	Later sampling revealed significant reductions in Pb measurements in lichen (about 3-5 fold) compared to initial samples	Air monitors within both National Parks, which report Pb-PM2.5 (EPA AirData website). This monitoring network (IMPROVE) has generally operated from 1985-present data, although data may not be available until 2004-05 for these sites.
Six peat core survey sites were sampled in 2013 and 2014 in Northern Alberta, Canada (Shotyk et al. 2016; draft ISA, Appendix 11, Section 11.3.2)	1910-2014	Peak accumulation rates between 1950 and 2000 in each sample, and overall decreasing rates of Pb accumulation were observed since 1980.	Pb accumulation rates coincide with the introduction of unleaded gasoline in the US and Canada in the mid-1970's. The uppermost, most recent, peat layers show near-zero modern atmospheric Pb deposition in the Alberta peat bogs. Sampling sites are in largely rural areas.

[A] As stated by the authors, "Surprisingly, we have observed that the lead concentrations were influenced by some physiological mechanisms (radial mobility) in red spruce and pine trees, whereas their cadmium and zinc concentrations were useful to infer air pollution chronology. Opposite patterns, integrity for lead concentrations but translocation for cadmium and zinc, were observed in the two studied beech stands. The results obtained clearly show that all analyzed indicators cannot be used together in any of the investigated tree species. For that reason, we recommend combining several tree species to study past air pollution history, as this approach can provide complementary information to reconstruct the environmental perturbations." (Doucet et al., 2012).

Table 3-4. Studies describing temporal trends in Pb in sediments of freshwater lakes.

Study Description	Time Period Covered	Description of Temporal Trends	Notes
Sediment core samples in small lake near Williamsburg, VA (Balascio 2019 ; draft ISA, Appendix 1, Section 1.2.7)	Core samples estimated to represent sediments accumulated since approximately 1700, when the lake was formed.	Pb concentrations continued to increase during the 1900s to a peak maximum in 1975 followed by a sharp decline	Pb deposition rates reflect the rise and fall of coal combustion, smelting, and leaded gasoline. Study location is in relatively urban area, having originally been used as a mill pond, and the site likely has received Pb inputs from media aside from air deposition.
Sediment core samples of 14 lakes in 8 National Parks in the US (Landers et al. 2010; draft ISA, Appendix 11, Section 11.1.3 and 2013 ISA, Section 2.6.2)	1850-2000	In parks in the conterminous US, Pb showed significant enrichment in all sediment profiles, and most lakes showed a peak between 1960 and 1980, with a decrease afterwards. In 4 Alaska lakes, Pb only showed modest enrichment starting in the 1920s.	Air monitors are present within the bounds of the National Parks surveyed in this study and are available on the AirData EPA website.
Sediment cores from two high-altitude lakes in the Adirondack Mountains in NY (Sarkar et al. 2015; draft ISA, Appendix 1, Section 1.2.7)	1880-2007	Concentration of Pb peaked in 1973 in both lake cores, and have since dropped 64% (West Pine Pond site) and 50% (Clear Pond site) since ~1980 at	Despite a 94% drop in national lead emissions since 1980s, authors theorize the less dramatic decline in Pb flux data could be release of legacy Pb stored in watershed soils that bias recent sedimentary Pb concentrations. Study sites are in remote locations and are likely to have deposition from ambient air as primary source of Pb input.
Sediments in lakes in multiple lakes across New York, New England and Nova Scotia (Dunnington, 2020; draft ISA, Appendix 1, Section 1.3.3.4)	1800-2000	Pb dating reveals anthropogenic Pb concentrations began increasing first in the Adirondack region in 1859 followed by the VT-NH-ME region in 1874, and finally in Nova Scotia in 1901. Pb declines sharply after 1980.	Lakes sampled have long history of anthropogenic uses, and may have Pb inputs from multiple media pathways.

Table 3-5. Studies describing temporal trends in Pb in marine biota.

Study Description	Time Period Covered	Description of Temporal Trends	Notes
Long term sampling in California coast from as part of National Mussel Watch (NMW) and CA State Mussel Watch (CSMW) (Melwani et al. 2014; draft ISA, Appendix 11, Section 11.4.2)	1977-2010	In NSW, 11 of 35 sites saw decreasing Pb levels and in CSMW, 8 of 21 sites saw decreasing Pb levels in metal concentration. No significant trends found in remaining sites.	Declines likely reflect changes in multiple sources, including surface water discharges and atmospheric Pb from historic gasoline and industrial sources. Study locations are in highly urbanized areas and likely received Pb input from numerous media pathways.
Shell collection off coastal NC in 1980, 1982, 2002, and 2003 (Gillikin et al. 2005; draft ISA, Appendix 11, Section 11.4.2)	1942-2002	Pb/Ca rations in shells peaked near 1980 and decreased until the conclusion of sampling in 2003.	Annual average Pb/Ca ratios were estimated from 1942-2002 using concentration measurements milled between the mollusk shell growth lines, which provide corresponding chronological measurements. Study locations include both urban and rural areas.
Study examined Pb concentrations in horseshoe crab eggs (Burger and Tsipoura 2014; draft ISA, Appendix 11, Section 11.4.2)	1993, 1994, 1995 and 1999, 2000, and 2012	General decline in Pb over time in a comparison of compiled data from earlier surveys (the 1993-1995) and the later surveys (1999-2012).	Some of the individual resampled sites showed a clear temporal decrease in Pb from earlier surveys to later ones, while at other locations the temporal Pb concentration trend was more variable. Samplings sites in the Delaware Bay likely have multiple pathways of Pb input.
Bivalve shell analysis off coastal VA (Krause-Nehring et al. 2012; draft ISA, Appendix 11, Section 11.4.2)	1775-2006	General patter of continuous increase in Pb concentration after 1910, peaking in 1979, and then declining to pre-1930 values after 2000.	The elevated shell Pb corresponded to the period of peak Pb gasoline use in the US, with Pb deposition to the offshore site including atmospheric transport by easterly winds. Sampling sites in VA likely have multiple pathways of Pb input.

3.2.2 Exposure Assessment Tools and Factors Affecting Pb Bioavailability

In considering the currently available information with regard to evaluation of potential risk associated with air-related ecosystem exposures, we give attention to the following question:

- Are there updates to or additional information regarding available risk screening tools, such as soil screening levels, or ambient water and sediment quality criteria?

Current research on bioavailability and speciation of Pb continues to describe the complexity of Pb bioavailability in ecosystems and the associated challenges to describing toxicity (draft ISA, Appendix 11, sections 11.2.2, 11.3.2, and 11.4.2). As recognized in prior

reviews, a wide range of environmental factors affects the distribution of Pb in the environment and Pb bioavailability and, accordingly, Pb-induced toxicity and associated ecological risk (draft ISA, Appendix 11, section 11.1.6; 2013 ISA, section 2.6.1; 2006 AQCD, summarized in Section 8.7).

In regard to soil screening levels, the 2006 REA (screening assessment) had relied on Eco-SSLs, which are maximum contaminant concentrations in soils that are predicted to result in little or no quantifiable effect on terrestrial receptors (draft ISA, Section 11.1.7.2). In that application of the Eco-SSLs, that assessment noted appreciable uncertainty regarding the avian Eco-SSLs. The draft ISA for the current review identifies a study proposing an update to the avian Eco-SSL based on re-analysis of the study used in the initial 2005 derivation (Sample 2019).

The current and past evidence documents that a wide range of environmental factors affects the distribution of Pb in the environment and Pb bioavailability and, accordingly, Pb-induced toxicity and associated ecological risk (draft ISA Appendix 11, Section 11.1.6; 2013 ISA, Section 6.2.1; 2006 AQCD, Section 8.7). The draft ISA discusses the current evidence regarding various aspects of Pb bioavailability and impacts on toxicity. In terrestrial and freshwater systems, complexities related to the differences in the many interacting determinants of bioavailability and the difficulty of identifying and quantifying those interactions have complicated capabilities for predictive response modeling (draft ISA, section 11.1.6). Since the 2006 screening assessment, there has been some development and refinement of models that predict toxicity by incorporating factors affecting bioavailability, which have advanced the field of metals risk assessment.

With regard to aquatic ecosystems, the draft ISA notes that the "physicochemical composition of the receiving water determines the bioavailability and thus the toxicity of metals to aquatic organisms" (draft ISA, section 11.1.6). Accordingly, bioavailability models for aquatic systems incorporate water chemistry. For example, the Biotic Ligand Model (BLM), which predicts both the bioaccessible and bioavailable fraction of Pb in the aquatic environment, is described as predicting toxicity of metals, including Pb, for a large range of water quality conditions and with the consideration of metal-ligand complexation and as having potential for estimating the importance of environmental variables such as dissolved organic carbon in limiting uptake of metals by aquatic organisms. (draft ISA, section 11.1.6). Other approaches to describing and predicting bioavailability and subsequent toxicity of metals in aquatic environments include empirically based multiple linear regression models, which take into consideration a wide range of endpoints and water chemistry parameters from large empirical toxicity datasets (draft ISA, section 11.1.6; Brix et al., 2020). Such models are suggested to have

some advantages over the BLM in adjusting for water chemistry in the context of ambient water quality criteria (draft ISA, section 11.1.6).

There continue to be challenges affecting our ability to predict Pb exposure responses in terrestrial systems, primarily due to much of the experimental toxicity data for terrestrial organisms utilizing soil spiked with soluble Pb salts for dosing. In this regard, the draft ISA notes a recent study has suggested applying empirically derived adjustments to results from laboratory experiments using soils spiked with Pb in soluble laboratory salts to account for variation in toxicity observed in the field due to percolation and aging, as well as differences in toxicity that arise from differing soil properties (draft ISA, section 11.1.6). Such an approach, if evaluated further, may be useful for addressing a limitation of Eco-SSLs, some of which are lower than background soil Pb concentration (draft ISA, section 11.2.5).

3.3 KEY OBSERVATIONS AND INITIAL PLANS FOR THE CURRENT REVIEW

In considering the question as to whether the currently available evidence provides support for new evaluations or reduced uncertainty in past analysis so as to inform our understanding of welfare risks associated with air quality under the current Pb secondary standard, we reflect on the information discussed in the preceding sections. As an initial matter, we look to the case study that was most informative in the last two reviews (HBEF). Additionally, we consider the potential for additional analyses or investigations of information available in this review to also prove informative to judgments regarding the existing standard in the current review. We conclude that limitations remain in available datasets and in multimedia fate, transport, exposure and toxicity modeling tools for Pb that preclude the conduct of a comprehensive predictive risk assessment for ecological effects of air-related Pb without substantial uncertainty. Rather for the purposes of quantitative analyses in this review, we judge it appropriate to continue to consider the findings of the HBEF case study and to also investigate long-term non-air media datasets in more remote areas (with little influence of non-air sources) with regard to potential for quantitative relationships of non-air media concentrations with air Pb concentrations that may inform consideration of multimedia responses to air quality conditions under the current Pb standard.

With regard to the HBEF case study, we note that it continues to be provide informative evidence regarding the consideration of atmospherically derived Pb effects on an ecologically vulnerable ecosystem. Conclusions regarding this case study included that there was “little evidence that sites affected primarily by long-range Pb transport [such as this one] have experienced significant effects on ecosystem structure of function” (2006 AQCD, p AX-98). At the time of the last review, it was considered unlikely that conditions would have appreciably

changed from that of the data available through 2000 on which the previous conclusions were based, such that the ambient air concentrations under air quality conditions associated with meeting the standard were judged unlikely to directly impact stream Pb levels (81 FR 71938). In planning so far in this review, we have conducted searches of the ambient air monitors[24] for air Pb monitors that could provide a historical record of ambient air lead concentrations in the areas near the HBEF. The search did not, however, reveal any nearby monitors operating during the time period in which HBEF Pb deposition data was collected. In further consideration of this case study data set in this review, it may be appropriate to investigate the potential for a more distant Pb monitor to act as surrogate in a way that may be informative to consideration of protection offered by the existing standard.

As evidenced by the discussions above, in this review, as in the last review, we face complications in estimating environmental Pb concentrations and exposures associated with the current standard and associated welfare risks. However, in the discussion above we have identified some datasets that we plan to investigate that may update our understanding in these areas in a way that will contribute to conclusions regarding public welfare protection afforded by the current standard. More specifically, we plan to investigate the potential for discerning status of current environmental concentrations with regard to dependence on (or influence of) current ambient air concentrations through evaluation of trend studies.

The temporal trends studies listed in Tables 3-3 through 3-5 presented little data on ambient air concentrations of Pb concurrent with the non-air media measurements, limiting our ability to conduct a full quantitative analysis of the relationship between deposition rates and ambient air concentrations. Investigation of the availability of air Pb monitors near locations of these trends' studies, however, may yield data that could inform our understanding of relationships between ambient air concentrations of Pb, deposition and concentrations in other media. A preliminary search for air monitors within the vicinity of these study locations reveals potential availability of this type of data. Where such data may exist, consideration will be needed on a number of factors, including distance of the air Pb monitor from a study location, monitoring time period, sample frequency and the type of air Pb monitor (i.e., Pb-TSP, Pb-$PM_{2.5}$).

A preliminary investigation was conducted using the EPA AirData Air Monitoring website to explore the possibility of looking at relationships between relevant proximity air monitor concentrations and study sites for which historical Pb concentration data are available. Air monitoring data available on the AirData website include from monitors within the SLAMS,

[24] The EPA maintains a mapping application that facilitates searching for all ambient air monitors for which air monitoring data is available in the EPA Air Quality System (https://www.epa.gov/outdoor-air-quality-data).

CSN, IMPROVE, and NAATS networks (as described in IRP, V1, Appendix A). For this investigation we focused on studies that included rural sites with limited potential for environmental Pb releases other than atmospheric. The following studies were identified as involving generally rural locations, with potentially relevant air monitors available. In further analysis for consideration in the PA, we intend to investigate the availability of data from these monitors for the time period of the study, and the possibility of Pb data from the monitors proving useful to the evaluation of potential relationships between the air Pb and non-air media, including with regard trend comparisons.

- Richardson et al. (2014). This study described a regional survey of forest floor soils sampled in Northeastern US (PA, NY, NH, MA, VT, and CT).
- Sarkar et al. (2015). This study presented sediment core data, with dating, from two high-altitude lakes in the Adirondack Mountains in NY.
- Landers et al. (2010). This study collected sediment core data of 14 lakes in 8 National Parks in the U.S.
- Landers et al. (2008). This study reported on Pb concentrations in Lichen from Golden Lake in Mount Rainier National Park (2005) and Emerald Lake Basin in Sequoia/Kings National Parks (2004).

Analyses developed in this review will be described in the PA, with details documented in appendices or accompanying volumes, as appropriate. We expect to also consider in the PA any analyses from the last review that we do not update in this review but that are still informative to this review when viewed in the context of the currently available evidence as characterized in the ISA and of updated air quality and other analyses performed for this review. Accordingly, the PA will include description and discussion of all analyses being considered of in this review, both those newly developed in this review as well as analyses from the last review for which an updated assessment was not performed but that are still informative for this review. The draft PA will be released for public comment and provided to the CASAC for its review. Advice and comments received will be considered in completing the final version of the quantitative analyses and information considered in the policy evaluations presented in the final PA.

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Appendix: Cumulative Exposure Estimates for Different Birth Cohorts

SUMMARY

Blood Pb is an indicator of Pb that is distributing through an individual at a point in time, and, accordingly, may best reflect recent exposures. It cannot, however, reflect an individual's exposure history. Given the role of bone as a repository for Pb once in the body, bone Pb is considered to provide a measure of an individual's cumulative lifetime exposure. Additionally, where longitudinal blood Pb measurements are available, a cumulative blood Pb metric is also informative regarding an individual's exposure across their lifetime. A cumulative blood Pb metric may be derived in a manner conceptually similar to a cumulative exposure metric often employed in worker studies (e.g., using ppm-days). The metric is derived essentially by multiplying blood Pb measurement by years to which it is applied yielding an index in terms of (µg/dL)·yrs (e.g., Nie et al., 2011 and Somervaille et al., 1988).

Given the backdrop of dramatic reductions in Pb exposures over the past four plus decades, as evidenced in blood Pb levels of young children during that time, adults in the U.S. population have significant Pb exposure histories. Further, adults of different ages may have appreciably different exposure histories. This can be illustrated through use of a cumulative blood Pb index (CBLI), a metric sometimes used as an exposure metric in epidemiological studies of adult populations (2013 ISA, section 3.3.5; Nie et al., 2011; Hu et al., 2007; Somervaille et al., 1988).

The CBLI is calculated as:

$$CBLI = \sum_{i=1}^{n} 0.5 \times (PbB_{i+1} + PbB_i) \times (t_{i+1} - t_i)$$

Where blood Pb_i and blood Pb_{i+1} are the blood Pb concentrations at two consecutive times t_i and t_{i+1} and t_1 and t_N are the beginning and ending time for the blood lead measurements (Nie et al., 2011). Using NHANES blood Pb, CBLI was estimated for four birth cohorts (1945, 1970, 1990 and 2010). The CBLI estimates for different birth cohorts (See Tables 1-2 and 1-3 above) illustrate the appreciably different Pb exposures that adults in today's population have experienced and the difference of those exposures from adults of tomorrow.

ANALYTICAL APPROACH

NHANES data (Table A-1) are used to develop age-specific CBLI estimates for four birth cohorts: 1945, 1976, 1990 and 2010 (Table A-2). Since 1976, the CDC has been monitoring blood Pb levels nationally through the NHANES that provides nationally representative biomonitoring data for Pb. NHANES is designed to assess the health and nutritional status of the civilian noninstitutionalized U.S. population and is conducted by the National Center for Health Statistics, part of the Centers for Disease Control and Prevention. NHANES conducts interviews

and physical examinations with a nationally representative sample of approximately 10,000 people in each two-year year survey cycle. CDC's National Center for Environmental Health measures concentrations of environmental chemicals in blood and urine samples collected from NHANES participants. Summaries of the measured values are provided in the Fourth National Report on Human Exposure to Environmental Chemicals (CDC, 2021).

Because the blood Pb monitoring began in 1976, there are data gaps (particularly for years prior to the first NHANES) and surrogate assignments are employed. CBLIs are estimated for all cohorts up to 2018 using the most recently available NHANES (2017-2018). The projected CBLI estimates were also calculated for the years beyond 2028 for the 1990, 2010 and 1970 cohorts. In general, the following approaches were used to assign blood Pb levels each year for the four birth cohorts:

- For years prior to the 1st NHANES, the results for the relevant age(s) from the 1st survey are used.
- For years subsequent to the last NHANES, the results for the relevant age(s) from the last survey are used.
- For years intermediate to existing NHANES, there's a bridging of the results for the two closest NHANES are used (see notes in Table A-2 below for specific details).

A similar approach used NHANES data (Table A-3) to estimate the CBLI for three Non-Hispanic Black cohorts, born in 1990, 2000 and 2010 (Table A-4).

KEY LIMITATIONS AND UNCERTAINTIES

There are a number of inherent limitations and associated uncertainties in the analytical approach described above (and in the notes section of Table A-2). Several of importance are summarized here.

- Reliance on the NHANES blood Pb level estimates presumes those surveys appropriately reflect national average blood Pb measurements.
- The use of first NHANES in assigning blood Pb levels in years before 1976 contributes uncertainty to the yearly blood Pb estimates and associated CBLI estimates. The blood Pb assignments, and associated CBLI, for the 1945 and 1970 cohorts may be underestimated, to the extent exposures were higher in years prior to 1976 from the widespread use of leaded gasoline and other sources.
- The use of readily available NHANES estimates, which were limited with regard to separate age groups for adults, resulted in the use of NHANES reported estimates for all adults 20 years or older, rather than for adult age subgroups. This will have contributed uncertainty, with different bias for different ages.
- The recently available publication by Wang et al. (2021) reports geometric means from NHANES from 1999 to 2016 for birth cohorts of the 1940s, 50s, 60s, 70s , 80s, and 90s. These reported values for the 1940s cohort indicate that the estimates applied to the 1945 cohort in Table A-2 may be slight underestimates. This would contribute

to a low bias for the 1945 cohort CBLI estimate for ages older than 50 years. Use of Wang et al. (2021) in future iterations of this analysis may reduce some uncertainties in CBLI estimates associated with assignments of blood Pb levels to older ages.

- Given the current trajectory of declining blood Pb levels, the use of 2017-2018 NHANES blood Pb levels in assigning blood Pb levels for subsequent years in the 1970, 1990, and 2010 cohorts may contribute to overestimates in estimates of exposure (and accordingly, CBLI estimates) for those years.

Table A-1. Geometric Mean Blood Pb Levels (BLL) for the general population.

Year	1-2 yr	3-5 yr	1-5 yr	6-8 yr	9-11yr	6-11 yr	12-14yr	15-17yr	12-19yr	18-24yr	> 20	20-49yr	20-64yr	25-34yr	35-44yr	45-54yr	55-64yr	65-74yr	> 65	50-69yr	> 70	Women 15-49yrs	All ages
1976-1980 median	15.7	14.9	15.2	13.1	12.3	12.7	11.4	12.1		13.1				13.7	14.6	15.3	14.6	14.4				10.37	
1988-1991	4	3.3	3.6	2.5	2.3	2.4			1.6			2.6								4	4	1.85	
1991-1994	3.1	2.5	2.7	2.1	1.8	1.9			1.5			2.1								3.4	3.4	1.53	
1995-1998	2.7	2.2	2.3	1.8	1.6	1.7																	
1999-2002	2.2	1.8	1.9	1.4	1.3	1.4																1.05	
1999-2000			2.23			1.51			1.1		1.75												1.66
2001-2002			1.7			1.25			0.942		1.56												1.45
2003-2006	1.8	1.5	1.6	1.2	1.1	1.1																0.91	
2003-2004			1.77			1.25			0.946		1.52		1.45						2.07				1.43
2005-2006			1.46			1.02			0.797		1.41		1.31						2.1				1.29
2007-2010	1.5	1.2	1.3	1	0.8	0.9																0.81	
2007-2008			1.51			0.988			0.8		1.38		1.3						1.91				1.27
2009-2010			1.17			0.838			0.68		1.23		1.16						1.71				1.12
2011-2016	0.9	0.8	0.8	0.7	0.6	0.6																0.61	
2011-2012			0.97			0.681			0.554		1.09		1.02						1.6				0.973
2013-2014			0.782			0.567			0.506		0.967												0.858
2015-2016			0.758			0.571			0.467		0.92												0.82
2013-2016																							
2017-2018			0.67			0.475			0.411		0.855												0.753

GM (Geometric Mean) for all ages from NHANES and published reports. BLL values are color coded to match the corresponding reference.

Interpolated GMs averaged values for 1991-94 and 1999-2002.

GM for ages 1-5, 6-11, 12-19, and 20+ for the year 2017-2018 obtained from CDC Early Release of BLL from NHANES

GMs for age 1 thru 11 (4-yr periods: 1976-80, 1988-91, 1991-94, 1999-2002, 2003-05, 2007-10, 2011-16 6) from Egan et al., 2021

GMs (2 yr periods: 2003-2016) for ages 20-64 and >=65 from Jain, 2016a and GM 1-19 yrs (2003-2012) Jain 2016b

Medians for ages 12-74 (1976-1980) from Mahaffey et al., 1982

GMs for age 1-19 and > 20 (2-yr periods) from CDC, 2018

GMs for age 12 to > 70 (1991-1994) from Pirkle et al., 1998

GMs for age 12 to > 70 (1988-1991) from Brody et al., 1994

GMs for women, ages 15-49 (4-yr periods) from Ettinger et al., 2020

Table A-2. Estimated Cumulative CBLI based on NHANES GM estimates for four general population cohorts.

	2010 Cohort				1990 Cohort				1970 Cohort				1945 Cohort			
Age	Year	Age	GM BLL ug/dL	CBLI µg/dL ·yrs	Year	Age	GM BLL ug/dL	CBLI µg/dL ·yrs	Year	Age	GM BLL ug/dL	CBLI µg/dL ·yrs	Year	Age	GM BLL ug/dL	CBLI µg/dL ·yrs
	2010	0	0.81		**1990**	0	1.85		**1970**	0	10.37		**1945**	0	10.37	
	2011	1	0.97	0.9	1991	1	4	2.9	1971	1	15.7	13.0	1946	1	15.7	13.0
	2012	2	0.97	1.9	1992	2	3.1	6.5	1972	2	15.7	28.7	1947	2	15.7	28.7
	2013	3	0.8	2.7	1993	3	2.5	9.3	1973	3	14.9	44.0	1948	3	14.9	44.0
	2014	4	0.8	3.5	1994	4	2.5	11.8	1974	4	14.9	58.9	1949	4	14.9	58.9
5	**2015**	**5**	**0.8**	**4.3**	**1995**	**5**	**2.5**	**14.3**	**1975**	**5**	**14.9**	**73.8**	**1950**	**5**	**14.9**	**73.8**
	2016	6	0.6	**5.0**	1996	6	2.1	**16.6**	1976	6	13.1	**87.8**	1951	6	13.1	**87.8**
	2017	7	0.475	5.6	1997	7	1.8	18.5	1977	7	13.1	100.9	1952	7	13.1	100.9
	2018	8	0.475	6.1	1998	8	1.8	20.3	1978	8	13.1	114.0	1953	8	13.1	114.0
	2019	9	0.475	6.5	1999	9	1.3	21.9	1979	9	12.3	126.7	1954	9	12.3	126.7
10	**2020**	**10**	**0.475**	**7.0**	**2000**	**10**	**1.3**	**23.2**	**1980**	**10**	**12.3**	**139.0**	**1955**	**10**	**12.3**	**139.0**
	2021	11	0.475	7.5	2001	11	1.3	24.5	1981	11	12.3	151.3	1956	11	12.3	151.3
	2022	12	0.411	7.9	2002	12	0.942	25.6	1982	12	11.4	163.2	1957	12	11.4	163.2
	2023	13	0.411	8.3	2003	13	0.946	26.5	1983	13	11.4	174.6	1958	13	11.4	174.6
	2024	14	0.411	8.7	2004	14	0.946	27.5	1984	14	6.5	183.5	1959	14	11.4	186.0
	2025	15	0.411	9.2	2005	15	0.797	28.4	1985	15	1.6	187.6	1960	15	12.1	197.7
	2026	16	0.411	9.6	2006	16	0.797	29.2	1986	16	1.6	189.2	1961	16	12.1	209.8
	2027	17	0.411	10.0	2007	17	0.8	30.0	1987	17	1.6	190.8	1962	17	12.1	221.9
	2028	18	0.411	10.4	2008	18	0.8	30.8	1988	18	1.6	192.4	1963	18	13.1	234.5
	2029	19	0.411	10.8	2009	19	0.68	31.5	1989	19	1.6	194.0	1964	19	13.1	247.6
	2030	20	0.411	11.2	2010	20	0.68	32.2	1990	20	1.6	195.6	1965	20	13.1	260.7
21	**2031**	**21**	**0.411**	**11.6**	2011	21	0.68	32.9	1991	21	1.6	197.2	1966	21	13.1	273.8
	2032	22	0.411	12.0	2012	22	0.68	33.5	1992	22	1.6	198.8	1967	22	13.1	286.9
	2033	23	0.411	12.4	2013	23	0.68	34.2	1993	23	1.6	200.4	1968	23	13.1	300.0
	2034	24	0.411	12.9	2014	24	0.68	34.9	1994	24	1.6	202.0	1969	24	13.1	313.1
	2035	25	0.411	13.3	2015	25	0.68	35.6	1995	25	1.6	203.6	1970	25	13.7	326.5
	2036	26	0.411	13.7	2016	26	0.68	36.3	1996	26	1.6	205.2	1971	26	13.7	340.2
	2037	27	0.411	14.1	2017	27	0.68	36.9	1997	27	1.6	206.8	1972	27	13.7	353.9
	2038	28	0.411	14.5	2018	28	0.68	37.6	1998	28	1.6	208.4	1973	28	13.7	367.6
	2039	29	0.411	14.9	2019	29	0.68	38.3	1999	29	1.6	210.0	1974	29	13.7	381.3
30	**2040**	**30**	**0.411**	**15.3**	2020	30	0.68	39.0	2000	30	1.6	211.6	1975	30	13.7	395.0
	2041	31	0.411	15.7	2021	31	0.68	39.7	2001	31	1.56	213.2	1976	31	13.7	408.7
	2042	32	0.411	16.1	2022	32	0.68	40.3	2002	32	1.56	214.7	1977	32	13.7	422.4
	2043	33	0.411	16.6	2023	33	0.68	41.0	2003	33	1.45	216.2	1978	33	13.7	436.1
	2044	34	0.411	17.0	2024	34	0.68	41.7	2004	34	1.45	217.7	1979	34	13.7	449.8
	2045	35	0.411	17.4	2025	35	0.68	42.4	2005	35	1.31	219.1	1980	35	14.6	464.0
	2046	36	0.411	17.8	2026	36	0.68	43.1	2006	36	1.31	220.4	1981	36	14.6	478.6
	2047	37	0.411	18.2	2027	37	0.68	43.7	2007	37	1.3	221.7	1982	37	14.6	493.2
	2048	38	0.411	18.6	2028	38	0.68	44.4	2008	38	1.3	223.0	1983	38	14.6	507.8

	2010 Cohort				1990 Cohort				1970 Cohort				1945 Cohort			
Age	Year	Age	GM BLL ug/dL	CBLI µg/dL ·yrs	Year	Age	GM BLL ug/dL	CBLI µg/dL ·yrs	Year	Age	GM BLL ug/dL	CBLI µg/dL ·yrs	Year	Age	GM BLL ug/dL	CBLI µg/dL ·yrs
	2049	39	0.411	19.0	2029	39	0.68	45.1	2009	39	1.16	224.2	1984	39	*8.6*	519.4
	2050	40	0.411	19.4	2030	40	0.68	45.8	2010	40	1.16	225.4	1985	40	2.6	525.0
	2051	41	0.411	19.8	2031	41	0.68	46.5	2011	41	1.02	226.5	1986	41	2.6	527.6
	2052	42	0.411	20.3	2032	42	0.68	47.1	2012	42	1.02	227.5	1987	42	2.6	530.2
	2053	43	0.411	20.7	2033	43	0.68	47.8	2013	43	0.967	228.5	1988	43	2.6	532.8
	2054	44	0.411	21.1	2034	44	0.68	48.5	2014	44	0.967	229.4	1989	44	2.6	535.4
	2055	45	0.411	21.5	2035	45	0.68	49.2	2015	45	0.92	230.4	1990	45	2.6	538.0
	2056	46	0.411	21.9	2036	46	0.68	49.9	2016	46	0.92	231.3	1991	46	2.1	540.3
	2057	47	0.411	22.3	2037	47	0.68	50.5	2017	47	0.855	232.2	1992	47	2.1	542.4
	2058	48	0.411	22.7	2038	48	0.68	51.2	2018	48	0.855	233.0	1993	48	2.1	544.5
	2059	49	0.411	23.1	2039	49	0.68	51.9	2019	49	0.855	233.9	1994	49	2.1	546.6
50	**2060**	**50**	**0.411**	**23.5**	**2040**	**50**	**0.68**	**52.6**	**2020**	**50**	**0.855**	**234.8**	**1995**	**50**	**2.1**	**548.7**
									2021	51	0.855	235.6	1996	51	2.1	550.8
									2022	52	0.855	236.5	1997	52	2.1	552.9
									2023	53	0.855	237.3	1998	53	2.1	555.0
									2024	54	0.855	238.2	1999	54	1.75	557.0
									2025	55	0.855	239.0	2000	55	1.75	558.7
									2026	56	0.855	239.9	2001	56	1.56	560.4
									2027	57	0.855	240.7	2002	57	1.56	561.9
									2028	58	0.855	241.6	2003	58	1.45	563.4
									2029	59	0.855	242.4	2004	59	1.45	564.9
									2030	60	0.855	243.3	2005	60	1.45	566.3
									2031	61	0.855	244.2	2006	61	1.45	567.8
									2032	62	0.855	245.0	2007	62	1.45	569.2
									2033	63	0.855	245.9	2008	63	1.45	570.7
									2034	64	0.855	246.7	2009	64	*1.405*	572.1
									2035	65	0.855	247.6	2010	65	1.36	573.5
									2036	66	0.855	248.4	2011	66	1.36	574.9
									2037	67	0.855	249.3	2012	67	1.36	576.2
									2038	68	0.855	250.1	2013	68	1.36	577.6
									2039	69	0.855	251.0	2014	69	1.36	578.9
									2040	70	0.855	251.9	2015	70	1.36	580.3
									2041	71	0.855	252.7	2016	71	1.36	581.7
									2042	72	0.855	253.6	2017	72	1.36	583.0
									2043	73	0.855	254.4	2018	73	1.36	584.4
									2044	74	0.855	255.3	2019	74	1.36	585.7
75								**Age 75**	**2045**	**75**	**0.855**	**256.1**	**2020**	**75**	**1.36**	**587.1**

*** Approach:**
Age 0 is assigned maternal BLL (women age 15-49 from Ettinger et al., 2020) for relevant time period
For ages less than 20, cohorts are generally assigned BLLs for their age group and year.
Red font indicates variation from this approach. Variations include the following:
A - For ages 20 through 30, for years subsequent to 1989, the NHANES value for ages 12-19 yr is used. This is because
the next age group (>=20) includes ALL ages greater than 20 (with multiple gas Pb exposure years) and thus would overestima
BLLs for twenty-somethings. Given the declining exposures backdrop, this approach is not likely to bias estimates.
B - When year is prior to NHANES, the cohort is are assigned BLLs from 1st NHANES according to age group.
C - For ages less than 20 occurring in years subsequent to the most recent NHANES (2018), the last NHANES value
for the relevant age group is assigned (also see note A).
D - For ages >=20 occurring in years after the most recent NHANES (2018), the last NHANES for that age is retained
for subsequent years. Given the current downward BLL trend, this approach is not believed to underestimate BLLs
and may lend an upward bias.
E - For years during the NHANES sampling period (1976-2018) for which age-specific values are uncertain, interpolation (red ita
is applied consistent with understanding that with constant (or declining) exposure, an individual's BLL would not
increase as they age (we note that NHANES generally shows higher adult [vs teen] BLLs due to older individuals with
higher past BLLs in that group). Where values are needed to bridge years between two NHANES, the central year
between the two estimates is assigned the average of the two values, the prior value is retained for prior years, and
the subsequent value is assigned for subsequent years. More specifically, in time periods between NHANES for which
we lack estimates for age/year combo (e.g., 1945 birth cohort, ages 36-43), we retain the last estimate for
the first half of period, take next match for latter half of period and use average of two for midpoint.
F - For 1970 birth cohort, BLLs for ages 22-30 (years 1992-2000) is set to 1.6, as interpolation toward the 2001 (age 31)
BLL from 2001-02 NHANES.
G - For 1945 birth cohort, BLLs for ages 60-68, method of note E is applied to bridge from BLL for >=20yr-olds in 2003-4
to >=61yr-olds in 2013-2016.

Table A-3. Geometric Mean Blood Pb Levels (BLL) for Non-Hispanic Black Populations (NHB) from NHANES.

Years	NHB Children, 6 mo-5 yr	NHB Children, 1-5 yr	NHB Children, 6-11 yr	NHB Children, 6-16yr	NHB, 18-74yr	NHB, 20-64yr	NHB, ≥ 65yr	NHB, ≥ 15yr	NHB women, 15-49 yr*	NHB, All Ages	NHB Men ≥ 15yr	NHB Women ≥ 15yr
1976-80 (Med)	20.9	20.3	16.2	14.8	15.5				11.52	15.7		
1988-1991		5.2	3.9						2.16			
1991-1994		4.3	3						1.75	2.8		
1999-2002		2.8	2						1.21			
1999-2000		3.08								1.87		
2001-2002		2.59								1.65		
2003-2006		2.4	1.6						1.03			
2003-2004		2.73	1.89			1.63	2.8			1.69		
2005-2006		2.12	1.35			1.39	2.46			1.39		
2007-2010		1.8	1.2						0.92			
2007-2008		1.94	1.31			1.39	2.33			1.39		
2009-2010		1.59	1.15			1.27	2.02			1.24		
2011-2016		1.1	0.8						0.61			
2011-2012		1.29	0.9			1.04	1.85			0.998		
2013-2014		0.98								0.871		
2015-2016		0.89								0.856		
2013-2016												
2017-2018										0.766		
2015-2018		0.8										

GMs for all ages from NHANES Reports and BLL values are color coded to match the corresponding reference.
GMs for age 1 thru 11 (4-yr periods: 1976-80, 1988-91, 1991-94, 1999-2002, 2003-05, 2007-10, 2011-16) from Egan et al., 2021
GMs (2 yr periods: 2003-2016) for age 20-64 & >=65 from Jain 2016a and GM 1-19 yro (2003-2012) Jain 2016b
Medians for age 12-74 (1976-1980) from Mahaffey et al., 1982 NEJM
GM for age 1-5, 6-11, 12-19, and 20+ for the year 2017-2018 obtained from CDC Early Release of BLL from NHANES (CAS # 7439-92-1)
GMs for women, 15-49 (4-yr periods) from Ettinger et al., 2020
GMs for age 1-19 & >=20 (2-yr periods) from CDC, 2018
GMs for age 1-5 from 1999-2016 from Teye et al., 2022
GMs for age 12 to GE70 (1991-1994) from Pirkle et al 1998

Table A-4.Estimated Cumulative Blood Lead Index (CBLI) based on Non-Hispanic Black Populations NHANES GM estimates in Table 3.

	2010 Cohort					2000 Cohort					1990 Cohort			
Age	Year	age	GM BLL	CBLI (ug/dL)·yrs		Year	age	GM BLL	CBLI (ug/dL)·yrs		Year	age	GM BLL	CBLI (ug/dL)·yrs
0	2010	0	0.92			2000	0	1.21			1990	0	2.16	
	2011	1	1.1	1.0		2001	1	2.59	1.9		1991	1	5.2	3.7
	2012	2	1.1	2.1		2002	2	2.59	4.5		1992	2	4.3	8.4
	2013	3	1.1	3.2		2003	3	2.73	7.2		1993	3	4.3	12.7
	2014	4	1.1	4.3		2004	4	2.73	9.9		1994	4	4.3	17.0
5	2015	5	1.1	5.4		2005	5	2.12	12.3		1995	5	4.3	21.3
	2016	6	0.8	6.4		2006	6	1.89	14.3		1996	6	3.2	25.1
	2017	7	0.8	7.2		2007	7	1.2	15.9		1997	7	3.2	28.2
	2018	8	0.8	8.0		2008	8	1.31	17.1		1998	8	2	30.8
	2019	9	0.8	8.8		2009	9	1.15	18.3		1999	9	2	32.8
10	2020	10	0.8	9.6		2010	10	1.15	19.5		2000	10	2	34.8

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