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

Volume 2: Planning for the Review and the Integrated Science Assessment

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

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U.S. Environmental Protection Agency

Office of Air Quality Planning and Standards
Health and Environmental Impacts Division
and
Center for Public Health and Environmental Assessment
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This document serves as a public information document and as a management tool for the U.S. Environmental Protection Agency's Center for Public Health and Environmental Assessment and the Office of Air Quality Planning and Standards in conducting the review of the national ambient air quality standards for lead. This document is being circulated to facilitate discussion with the Clean Air Scientific Advisory Committee and for public comment to inform the EPA’s consideration of the current review of the national ambient air quality standards for lead. It does not represent and should not be construed to represent an Agency determination or policy. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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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 Pb, and may serve as a reference for the public and the CASAC in their consideration of the subsequent two volumes. Volume 2 (this document) addresses the general approach for the review and planning for the integrated science assessment (ISA) and will be the subject of a consultation with the CASAC. This volume identifies policy-relevant issues in the review and describes key considerations in the EPA's development of the ISA. Volume 3 is the planning document for quantitative analyses to be considered in the policy assessment (PA), including exposure and risk analyses. 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 will generally coincide with that of the draft ISA and it will be the subject of a consultation with the CASAC at that time.

1 INTRODUCTION

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). This Volume (2) of the integrated review plan (IRP) contains the current plans for the general approach for the review, as well as key planning considerations for development of the integrated science assessment (ISA). The NAAQS review process provides an integrative assessment of relevant scientific information and will focus on key aspects of the NAAQS, including the basic elements of the standards: the indicator,[1] averaging time, form,[2] and level. These elements, which together serve to define each ambient air quality standard, are considered collectively in evaluating the protection to public health and public welfare afforded by the standards.

This document is the second of three volumes that will comprise the IRP for the Pb NAAQS review. Volume 1 includes introductory or background information on the legislative requirements for reviews of the NAAQS, an overview of the review process, background information on prior reviews of the criteria and standards for Pb and a summary of key aspects of the basis for the existing Pb NAAQS, key aspects of the existing ambient air monitoring requirements for Pb, and a summary of the status and projected schedule for the current review (U.S. EPA, 2022, henceforth referred to as Volume 1 of the IRP). Volume 2 (this document) presents the general approach for this review, the policy-relevant questions guiding the review, and the plans for the development of the ISA. Specifically, Chapter 2 of Volume 2 outlines the general approach of the NAAQS review and details a set of policy-relevant questions intended to focus this review on the critical scientific and policy issues. Chapter 3 of Volume 2 presents plans for the ISA, including the document organization, scope and specific scientific questions for consideration in light of the overarching policy-relevant questions for the review. Together, Volumes 1 and 2 provide the current information regarding this review of the Pb NAAQS. Volume 3 of the IRP, the planning document for quantitative analyses to be considered in the policy assessment (PA), will be developed with consideration of the availability of new evidence as identified in the development of the ISA. Accordingly, the public release of Volume 3 of the

[1] The "indicator" of a standard defines the chemical species or mixture that is to be measured in determining whether an area attains the standard. For example, the indicator of the current NAAQS for photochemical oxidants is O_3.

[2] 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. For example, the form of the annual $PM_{2.5}$ NAAQS is the three-year average of the weighted annual mean $PM_{2.5}$ concentrations, while the form of the current three-month Pb NAAQS is a three-month average concentration not to be exceeded during a three-year period.

IRP will generally coincide with that of the draft ISA and it will be the subject of a consultation with the CASAC at that time.

2 POLICY-RELEVANT ISSUES IN THE CURRENT REVIEW

The approach to considering the information available in this review of the current primary and secondary Pb standards is framed by a series of questions, the answers to which are intended to inform the Administrator's judgment as to whether the current standards provide the requisite protection of public health and public welfare, and his decisions as to whether to retain or revise these standards. The ISA and PA developed in this new review of the Pb NAAQS will provide the basis for addressing these questions. These assessments focus on policy-relevant scientific information and analyses intended to address key questions related to the adequacy of the standards.

The overarching question in each NAAQS review is:

- **Do the currently available scientific evidence and exposure/risk-based information support or call into question the adequacy of the protection afforded by the current standard(s)?**

As appropriate, a review also addresses a second overarching question:

- **What alternative standards, if any, are supported by the currently available scientific evidence and exposure/risk-based information and are appropriate for consideration?**

In considering these overarching questions in the PA, a series of key policy-relevant issues particular to a given review are addressed. As summarized in section 3.2 of Volume 1, the fact that Pb is a multimedia and persistent pollutant contributes complexities to the review of the Pb NAAQS. 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. The policy-relevant issues thus far identified for this review of the Pb standards are presented in sections 2.1 and 2.2 as series of questions. The primary standard is discussed in section 2.1 and the secondary standard in section 2.2.

2.1 REVIEW OF THE PRIMARY STANDARD

The approach planned for this review of the primary standard is fundamentally based on using the Agency's assessment of the current scientific evidence, quantitative assessments of exposures and/or risks, and other associated analyses (e.g., air quality analyses) to inform the Administrator's judgments regarding a primary standard that is requisite to protect

public health with an adequate margin of safety. This approach involves translating scientific and technical information into the basis for addressing a series of key policy-relevant questions using both evidence- and exposure-/risk-based considerations. This series of key questions related to the primary standard is presented below, in the context of the general approach for the review.

The approach planned for this review of the primary Pb standard will build on the substantial body of work developed during the course of the prior reviews and the associated conclusions, taking into account the more recent scientific information and air quality data now available to inform our understanding of the key-policy relevant issues in this review. Key aspects of the basis for the decision establishing the standard in 2008 and retaining it without revision in 2016 are summarized in Volume 1. The ISA, risk and exposure analyses (as warranted), and PA developed in this review will provide the basis for addressing the key policy relevant questions in the review, and these documents will inform the Administrator's decisions as to whether to retain or revise the primary Pb standard.

The final decision on the primary standard is largely a public health policy judgment by the Administrator.[3] Final decisions must draw upon scientific information and analyses about health effects and risks, as well as judgments about how to deal with the range of uncertainties that are inherent in the scientific evidence and analyses. Consistent with the Agency's approach across all NAAQS reviews, the approach of the PA to inform these judgments is based on a recognition that the available evidence generally reflects continuums that include ambient air exposures for which scientists generally agree that effects are likely to occur through lower levels at which the likelihood and magnitude of response become increasingly uncertain. This approach is consistent with the requirements of the NAAQS provisions of the Act and with how the EPA and the courts have historically interpreted the Act. These provisions require the Administrator to establish standards that are requisite to protect public health with an adequate margin of safety. In so doing, the Administrator seeks to establish standards that are neither more nor less stringent than necessary for this purpose. The provisions do not require that standards be set at a zero-risk level, but rather at a level that avoids unacceptable risks to public health, including the health of sensitive groups[4].

[3] Key aspects of the decisions made in the last review, including the Agency's consideration of important policy judgments concerning the scientific evidence and exposure/risk information and associated uncertainties and limitations, as well as the Administrator's public health policy judgments regarding an adequate margin of safety are summarized in section 3.3 of Volume 1 of this IRP.

[4] More than one population group may be identified as sensitive or at risk in a NAAQS review. The decision in the review of the primary standard will reflect consideration of the degree to which protection is provided for these sensitive population groups. To the extent that any particular population group is not among the identified sensitive groups, a decision that provides protection for the sensitive groups would be expected to also provide protection for other population groups.

Evaluations in the PA are intended to inform the Administrator's public health policy judgments and decisions. In so doing, the PA considers the potential implications of various aspects of the scientific evidence, the exposure/risk-based information, and the associated uncertainties and limitations. The Agency's consideration of the full set of evidence and information available in this review will inform the answer to the following initial overarching question for the review:

- **Do the currently available scientific evidence and exposure-/risk-based information support or call into question the adequacy of the public health protection afforded by the current Pb primary standard?**

In reflecting on this question, we will consider the available body of scientific evidence, assessed in the ISA and used as a basis for developing or interpreting risk/exposure analyses, including whether it supports or calls into question the scientific conclusions reached in the last review regarding health effects related to exposure to ambient air-related Pb. Information available in this review that may be informative to public health judgments regarding significance or adversity of key effects will also be considered. Additionally, the currently available exposure and risk information, whether newly developed in this review or predominantly developed in the past and interpreted in light of current information, will be considered, including the extent to which it may continue to support judgments made in the last review. Further, in considering this question with regard to the primary Pb standard, as in all NAAQS reviews, we give particular attention to exposures and health risks to at-risk populations.[5] In this review, this includes a focus on young children and on early childhood exposures.

Evaluation of the available scientific evidence and risk/exposure information with regard to this consideration of the current standard will focus on key policy-relevant issues by addressing a series of questions such as the following:

- Does the currently available evidence alter our previous conclusions regarding health effects associated with multimedia exposure related to levels of Pb occurring in the ambient air?
  - Does the current evidence continue to support blood Pb level as a useful indicator of Pb exposure and dose for purposes of characterizing Pb health effects, with well-recognized strengths and limitations? To what extent does the evidence suggest alternatives?

[5] As used here and similarly throughout this document, the term population (in the context of health and the primary standard) refers to persons having a quality or characteristic in common, such as a specific pre-existing illness or a specific age or life stage. Some populations may be at increased risk of health effects occurring with exposure to Pb as a result of any of a variety of factors, including genetic or developmental aspects, disease or smoking status, and factors related to socioeconomic status, reduced access to health care or increased exposure.

  - To what extent has new information altered scientific conclusions regarding the relationships between Pb in ambient air and Pb in children's blood?
  - To what extent is there new scientific evidence available to improve our understanding of the health effects associated with various time periods of Pb exposures at various stages of life?
  - With what exposure circumstances (duration and levels), and lifestages, do health effects of concern occur? Is there evidence of effects at exposure levels lower than previously observed and what are important uncertainties in that evidence?
  - Has new information altered our understanding of human populations that are particularly sensitive to the current low environmental Pb exposures, including air-related exposures? Is there new evidence on health effects beyond neurocognitive endpoints in children that suggests additional sensitive populations should be given increased focus in this review?
  - To what extent does the newly available evidence alter our understanding of the concentration-response relationships between Pb in children's blood and reduced IQ?
  - What are the important uncertainties associated with the policy-relevant aspects of the evidence available in this review?
  - What are the nature and magnitude of the estimates of air-related risks remaining upon just meeting the current Pb standard?
  - What is the level of confidence associated with estimates of air-related risk generated for simulations just meeting the current Pb standard?
  - What are the important uncertainties associated with any risk/exposure estimates? To what extent have important uncertainties identified in the last review been reduced and/or have new uncertainties emerged?
- To what extent are the air-related risks remaining upon just meeting the current Pb standard important from a public health perspective?

If the information in the current review suggests that revision of the current primary standard would be appropriate to consider, the PA will evaluate how the standard might be revised based on the available scientific information, air quality assessments, and exposure/risk information and will also consider what the available information indicates as to the health protection expected to be afforded by the current or potential alternative standards. Such an evaluation may consider the effect of revision of one or more elements of the standard (indicator, averaging time, level, and form), with the effect being evaluated based on the resulting potential standard and all of its elements collectively. Based on such evaluations, the PA would then identify potential alternative standards (specified in terms of indicator, averaging time, level, and form) intended to reflect a range of alternative policy judgments as to the degree of protection that is requisite to protect public health with an adequate margin of safety, as well as options for standards expected to achieve it. Evaluation of what revision of the standard might be

appropriate to consider would be framed by specific policy relevant questions such as the following:

- Does the currently available information call into question the identification of Pb-TSP as the indicator for Pb? Is support provided for considering a different indicator?
- Does the currently available information call into question the current averaging time? Is support provided for considering different averaging times for the standard?
- What does the currently available information indicate with regard to a range of levels and forms of alternative standards that may be supported, and what are the uncertainties and limitations in that information?
- What do the available analyses indicate with regard to exposure and risk associated with specific alternative standards? What are the associated important uncertainties? To what extent might such alternatives be expected to reduce adverse impacts attributable to Pb, and what are the associated uncertainties in the estimated reductions?

The approach to reaching conclusions on the current primary standard and, as appropriate, on potential alternative standards is summarized in general terms in Figure 2-1.

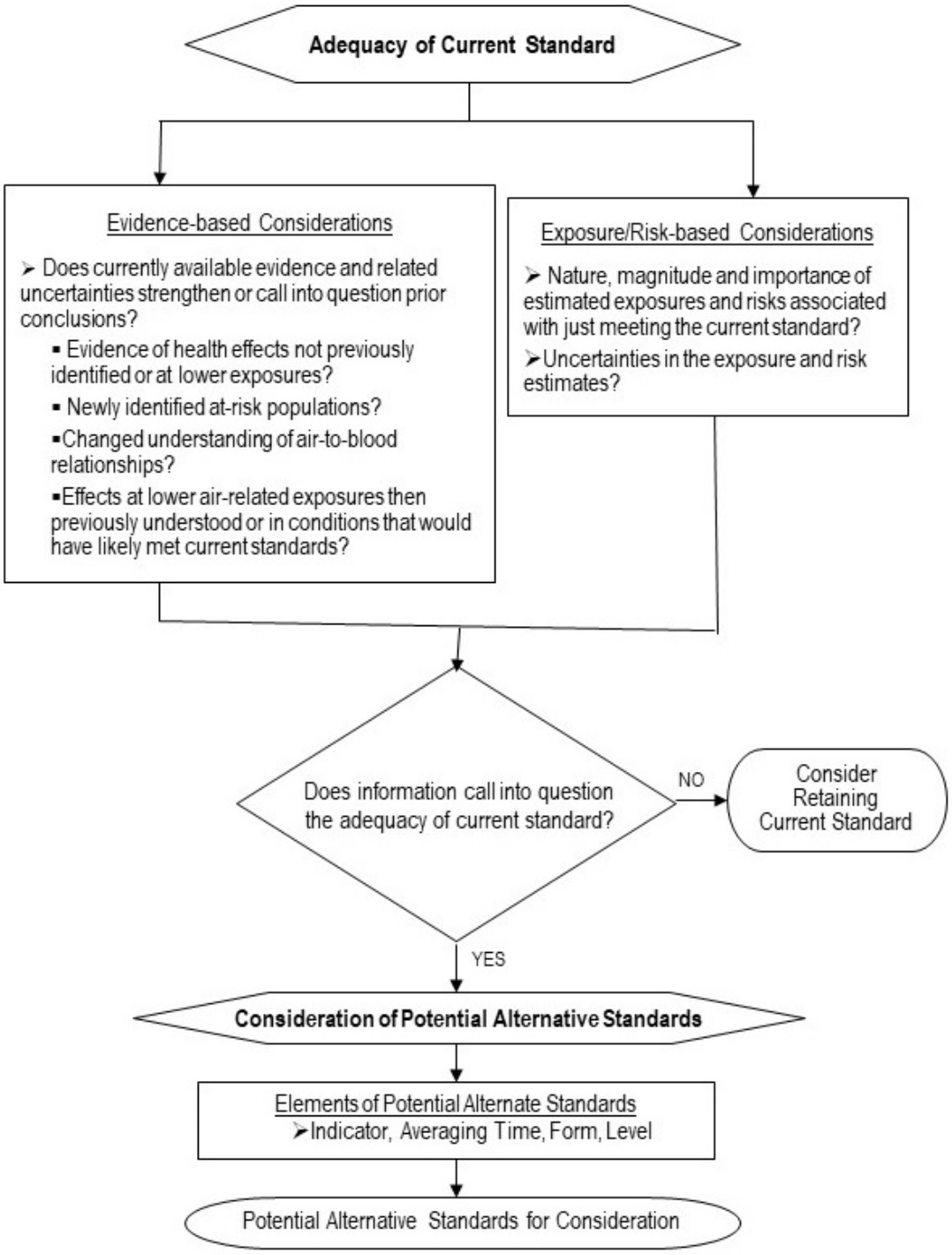

Figure 2-1. Overview of general approach for review of the primary Pb standard.

2.2 REVIEW OF THE SECONDARY STANDARD

The approach planned for this review of the secondary standard is fundamentally based on using the Agency's assessment of the current scientific evidence, quantitative assessments of exposures and/or risks, and other associated analyses (e.g., air quality analyses) to inform the Administrator's judgments regarding a secondary standard that is requisite to protect the public welfare from adverse environmental effects. This approach involves translating scientific and technical information into the basis for addressing a series of key policy-relevant questions using both evidence- and exposure-/risk-based considerations. This series of key questions related to the secondary standard is presented below, in the context of the general approach for the review.

The approach planned for this review of the secondary Pb standard will build on the substantial body of work developed during the course of prior reviews and on the associated conclusions, taking into account the more recent scientific information and air quality data now available to inform our understanding of the key policy-relevant issues in this review. The ISA, risk and exposure analyses (as warranted), and PA developed in this new review will provide the basis for addressing the key policy-relevant questions, and these documents will inform the Administrator's decisions as to whether to retain or revise this standard.

The final decision on the secondary standard is largely a public welfare policy judgment by the Administrator. Final decisions must draw upon scientific information and analyses about welfare effects and risks, as well as judgments about how to deal with the range of uncertainties that are inherent in the scientific evidence and analyses. Consistent with the Agency's approach across all NAAQS reviews, the approach of the PA to inform these judgments is based on a recognition that the available evidence generally reflects continuums that include ambient air exposures for which scientists generally agree that effects are likely to occur through lower levels at which the likelihood and magnitude of response become increasingly uncertain. This approach is consistent with the requirements of the NAAQS provisions of the Act and with how the EPA and the courts have historically interpreted the Act. The CAA provisions require the Administrator to establish secondary standards that are requisite to protect public welfare from any known or anticipated adverse effects associated with the presence of the pollutant in the ambient air. In so doing, the Administrator seeks to establish standards that are neither more nor less stringent than necessary for this purpose. The provisions do not require that secondary standards be set to eliminate all welfare effects, but rather to protect public welfare from those effects that are judged to be adverse.

Evaluations in the PA are intended to inform the Administrator's public welfare policy judgments and decisions. In so doing, the PA considers the potential implications of various aspects of the scientific evidence, the exposure/risk-based information, and the associated

uncertainties and limitations. The Agency's consideration of the full set of evidence and information available in this review will inform the answer to the following initial overarching question for the review:

- **Do the currently available scientific evidence and exposure/risk-based information support or call into question the adequacy of the public welfare protection afforded by the current secondary Pb standard?**

In reflecting on this question, we will consider the full body of available scientific evidence, assessed in the ISA and considered as a basis for developing or interpreting risk and exposure analyses, including whether it supports or calls into question the scientific conclusions reached in the last review regarding welfare effects related to ecosystem exposures to ambient air-related Pb. Information available in this review that may be informative to public policy judgments regarding significance or adversity of key effects on the public welfare will also be considered. Additionally, the currently available exposure and risk information, whether newly developed in this review or predominantly developed in the past and interpreted in light of current information, will be considered, including with regard to the extent to which it may continue to support judgments made in the last review. Further, in considering this question with regard to the secondary Pb standard, we give particular attention to exposures and risks for effects with the greatest potential for public welfare significance.

Evaluation of the available scientific evidence and risk/exposure information with regard to consideration of the current standard will focus on key policy-relevant issues by addressing a series of questions such as the following:

- To what extent has the newly available evidence altered our understanding of the movement and accumulation of air-deposited Pb through ecosystems over time?
  - Does this alter our understanding of Pb bioavailability in different media?
- Does the current evidence alter our conclusions from the last review regarding the nature of welfare effects associated with environmental exposures to Pb? Is there evidence on additional effects beyond those identified in the last review?
- Does the newly available evidence alter or further inform our understanding of the bioavailability of Pb in different types of ecosystems and media and the extent to which it affects toxicity or potential for effects?
- Does the newly available evidence indicate new exposure levels at which ecological systems or receptors are expected to experience effects?
- To what extent is there new information that improves our understanding of the portion of Pb existing in ecosystems today derived from ambient air or that would exist in response to ambient air Pb associated with the existing standard?

  - To what extent does the available information indicate that Pb-related effects are occurring as a result of multimedia pathways associated with ambient air conditions that would meet the current standard?
- What are the important uncertainties associated with the evidence available in this review? To what extent have important uncertainties identified in the last review been reduced and/or have new uncertainties emerged?
- With regard to the exposure/risk information, what are the nature and magnitude of exposure and risk related estimates for welfare effects associated with air quality conditions just meeting the current standard?
- What are the important uncertainties associated with interpretation of the exposure/risk information in this review and associated characterization of potential for public welfare effects? To what extent have important uncertainties identified in the last review been reduced and/or have new uncertainties emerged?
- To what extent are the estimates of exposures and risks associated with air quality conditions just meeting the current standard reasonably judged important from a public welfare perspective?
- What does the current evidence indicate regarding the air quality conditions (and associated atmospheric deposition) for which welfare effects might be expected? What is the public welfare significance of such impacts? What does the currently available information indicate regarding potential welfare impacts of air-related Pb and atmospheric deposition pathways associated with air quality conditions that meet the current standards?

If the information in the current review suggests that revision of the current secondary standard would be appropriate to consider, the PA will evaluate how the standard might be revised based on the available scientific information, air quality assessments, and exposure/risk information and will also consider what the available information indicates as to the public welfare protection expected to be afforded by the current or potential alternative standards. Such an evaluation may consider the effect of revision of one or more elements of the standard (indicator, averaging time, level, and form), with the effect being evaluated based on the resulting potential standard and all of its elements collectively. Based on such evaluations, the PA would then identify potential alternative standards (specified in terms of indicator, averaging time, level, and form) intended to reflect a range of alternative policy judgments as to the degree of protection that is requisite to protect public welfare from known or anticipated adverse effects, as well as options for standards expected to achieve it. Evaluation of what revision of the standard might be appropriate to consider would be framed by specific policy relevant questions such as the following:

- Does the currently available information call into question the identification of Pb-TSP as the indicator for Pb? Is support provided for considering a different indicator?

- Does the currently available information call into question the current averaging time? Is support provided for considering different averaging times for the standard?
- What does the currently available information indicate with regard to a range of levels and forms of alternative standards that may be supported, and what are the uncertainties and limitations in that information?
- What do the available analyses indicate with regard to exposure and risk associated with specific alternative standards? What are the associated important uncertainties? To what extent might such alternatives be expected to reduce adverse impacts attributable to Pb, and what are the associated uncertainties in the estimated reductions?

The approach to reaching conclusions on the current secondary standard and, as appropriate, on potential alternative standards is summarized in general terms in Figure 2-2.

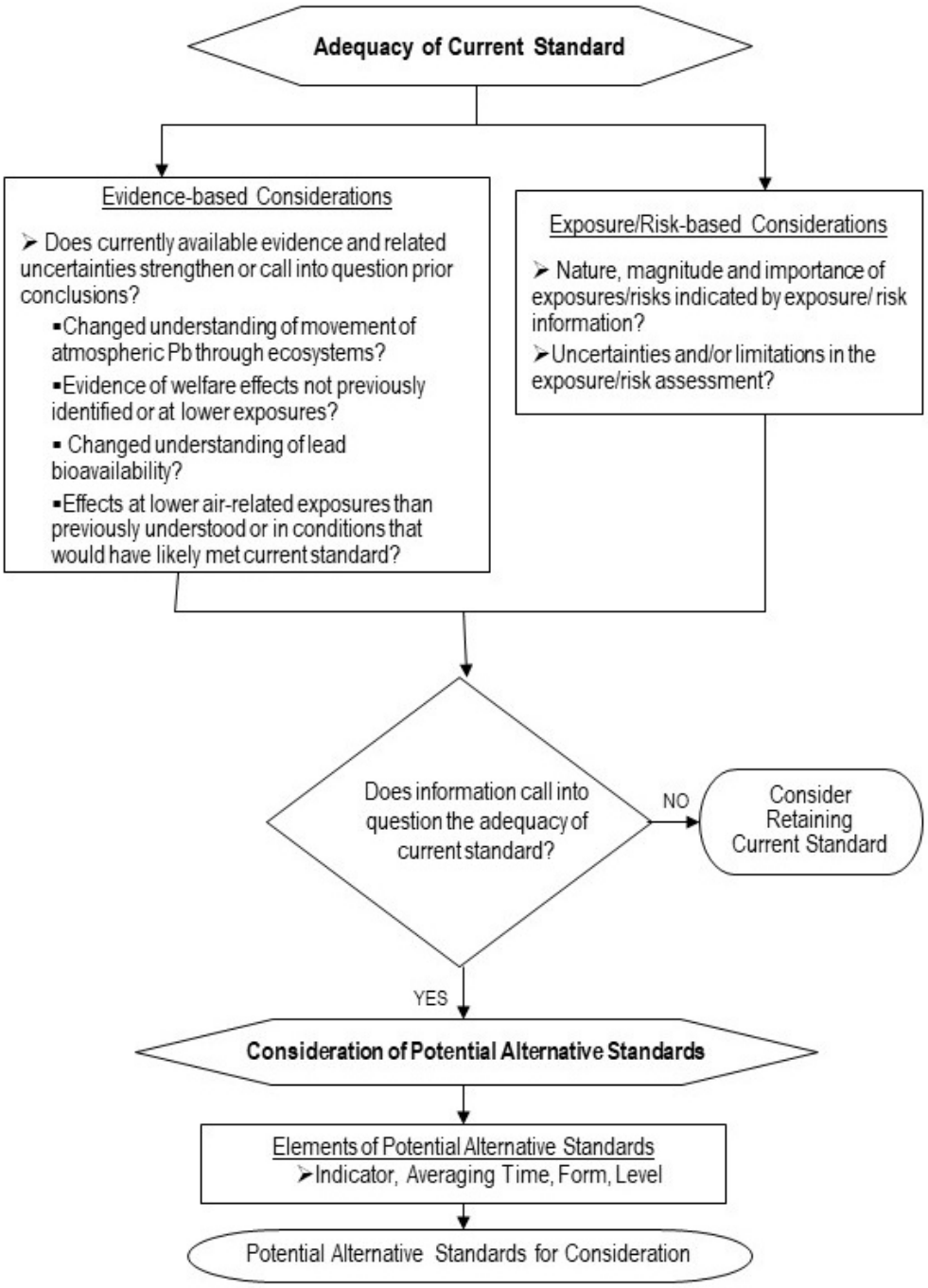

Figure 2-2. Overview of general approach for review of the secondary Pb standard.

3 DEVELOPMENT OF THE INTEGRATED SCIENCE ASSESSMENT

The ISA is developed to reflect the latest scientific information for characterization of the kind and extent of effects on public health or welfare which may be expected from the presence of the subject pollutant in ambient air. The content of the ISA in any NAAQS review provides the scientific basis for the EPA's decisions, in conjunction with additional technical and policy assessments, for the review of the NAAQS, as described in the Clean Air Act, section 108(a). General information on the legislative requirements of the air quality criteria and NAAQS, as well as an overview of the review process and the documents that comprise the review is presented in Volume 1 of the IRP.

An ISA is developed using the process outlined in the IRP, Volume 1, Appendix A. This process includes consideration of external peer input and review, as well as public comment. The following briefly summarizes the sequence of these steps. The first step is a public call for information, followed by a comprehensive literature search and screening process to identify policy-relevant literature published since the previous ISA. Draft materials for the ISA are subsequently prepared from the identified literature as well as literature available in previous reviews, taking into consideration the scientific questions presented in the ISA planning document. Following a peer-input step in which subject expert panelists provide feedback, the materials are updated, integrated, and used to evaluate causality relationships for health and ecological effects using the five-level causality determination hierarchy (described in Volume 1, Section A.4). Further, an integrative summary, the Integrative Synthesis, is drafted taking into consideration information from prior reviews as well as newly available evidence. The Integrated Synthesis is intended to provide a concise synopsis of the ISA conclusions and synthesis of key findings that best inform the review of the current Pb NAAQS with respect to health and welfare effects. The draft ISA, consisting of an Executive Summary, Integrative Synthesis, and associated appendices is then made available for review by the CASAC and the public. The final ISA is subsequently prepared based on consideration of CASAC advice and public comment.

This document, Volume 2 of the IRP, presents plans for the Pb ISA for the current review. Plans for the organization and scope of the ISA are summarized in sections 2 and 3, and specific policy-relevant questions related to the available scientific evidence that have been identified for consideration in the Pb ISA are described in the section 4. These questions were derived from the available science and associated uncertainties identified in the last Pb NAAQS review.

3.1 ORGANIZATION OF THE LEAD ISA

The general organization of the ISA for the current review will be consistent with that used in the ISA for Oxides of Nitrogen, Oxides of Sulfur, and Particulate Matter-Ecological Criteria (U.S. EPA 2020a) and the ISA for Ozone and Related Photochemical Oxidants (U.S. EPA 2020b). Accordingly, the ISA will begin with a Preface which summarizes key historical and legal aspects of prior Pb NAAQS reviews. An Executive Summary targeted to a wide range of audiences will succinctly summarize the conclusions of the ISA.

The Integrated Synthesis will serve as the main body of the ISA and provide a detailed summary of the key information for each topic area, including sources and environmental distribution; exposure, biomarkers, and toxicokinetics; conclusions regarding the nature of health and welfare effects associated with Pb exposure, including causality determinations for relationships between exposure to Pb and specific types of health and welfare effects; and identification of the human lifestages and populations at increased risk of the effects of Pb. The Integrated Synthesis will also discuss the evidence related to other policy-relevant issues, such as the exposure durations, metrics, and concentrations eliciting health and welfare effects; the concentration-response relationships for specific effects, including the overall shape and discernibility of thresholds in these relationships; and the public health and welfare impact of effects associated with exposure to Pb.

Appendices following the Integrated Synthesis will be organized by subject area, with the detailed assessment of the evidence for Pb sources and environmental distribution, exposure, health effects, and welfare effects presented in separate appendices. Each of the appendices will contain an evaluation of results from recent studies integrated with previous findings. Health appendices will include causality determinations describing the strength of the evidence between exposure to Pb and the health effect(s) of interest for a given Appendix [more detail on the types of causality determinations applied in the ISA is given in the Preamble to the ISAs (U.S. EPA, 2015) and in IRP Vol. 1, Section A.4]. Likewise, the appendix on welfare effects will conclude with causality determinations for the effects of Pb on terrestrial and aquatic biota and ecosystems.

3.2 SCOPE OF THE LEAD ISA

In the Pb ISA, the current scientific information will be evaluated in order to provide a better understanding of the health and welfare effects associated with exposure to ambient air-related Pb. In addition to the emphasis placed on health and welfare effects information, other scientific information will be identified and evaluated in order to provide a better understanding of the sources of Pb to ambient air, measurement and concentrations of Pb in ambient air, its subsequent fate and transport in the environment, pathways of human and ecological exposure, and toxicokinetic characteristics of Pb in the human body, as well as the characterization of population exposures to Pb.

Relevant literature published after the cutoff-date for the 2013 ISA (September 2011) will be considered for inclusion in the ISA. As described in section A.2.3. of Vol 1 of the IRP, journal articles, book chapters and reports included in the ISA must have undergone scientific peer review. In addition to the new literature, this ISA will build on and integrate evidence evaluated in prior assessments including the 2013 Pb ISA (U.S. EPA, 2013) and earlier assessments, e.g., Pb Air Quality Criteria Documents (AQCDs; U.S. EPA, 2006; U.S. EPA, 1986; U.S. EPA, 1977). Important studies from these previous reviews may be drawn on to reinforce key concepts and conclusions.[6] Older studies also may be the primary focus in some subject areas or scientific disciplines where research efforts have subsided, and/or where these older studies remain the definitive works available in the literature.

For air quality, atmospheric chemistry, fate, and transport the ISA will present and evaluate data related to ambient air concentration and size distributions of Pb, measured as a component of particulate matter. Any newly available information concerning air sources of freshly emitted Pb as well as on resuspension of historically released Pb will be discussed. Concentrations in ambient air have decreased significantly as reported in the routine national networks owing to controls enacted since the 1970s. The ISA will present and evaluate the latest data related to Pb source emissions and ambient air concentrations of Pb and will summarize and update spatial and temporal trends in Pb emissions and concentrations. In addition, it will summarize advances in our understanding of transport, transformation and deposition processes through air, soil, and water. The assessment will also include information about Pb network monitoring in the U.S. and advances in measurement methods, including new studies of Federal Reference Method and Federal Equivalent Method performance.

The exposure, toxicokinetics, and biomarkers appendix of the ISA will evaluate evidence developed since the last assessment that helps characterize relationships, and associated

[6] In so doing, any corrections to older studies will be incorporated (e.g., Kirrane and Patel, 2014; Lanphear et al., 2019).

variability and uncertainty, between ambient air Pb concentrations and human exposures to Pb relevant to the primary standard, and also recognize any limitations of the evidence in this area. A conceptual model of Pb exposure through various pathways, including exposure to airborne Pb and Pb deposited onto soil, as well as other air-related pathways, such as indoor dust and dietary contributions, will be included. The ISA will include a description of biomarkers of Pb exposure and current knowledge of the relationship between blood Pb levels and air Pb. The EPA will also assess and characterize evidence on blood Pb levels in different age groups and through time as Pb exposures have declined in the U.S. Discussion on biomarkers will also consider studies relevant to the assessment of errors in measurement or estimation of human exposure to Pb, as well as possible differential exposures of some populations.

In addition to characterizing routes of exposure, the ISA will also evaluate the literature relating to toxicokinetics of Pb; available models to evaluate its implications regarding the storage of Pb in the body; biological markers of Pb that indicate exposure and body burden; and the quantification of Pb dose from air-related exposure pathways (e.g., air-to-blood ratios). Uncertainties remained in the previous review regarding validation and application of biokinetic models, the blood Pb-air Pb relationship in slope-factor models, and the interpretation of blood Pb and bone Pb concentrations. The ISA will consider these key uncertainties and the extent to which new scientific evidence may inform our ability to characterize and/or reduce those uncertainties during the current review.

The scope of the health portions of the ISA is explicitly defined by scoping tools that generally define the relevant Population, Exposure, Comparison, Outcome, and Study Design (PECOS). The PECOS tool characterizes the parameters and provides a framework to aid in identifying the relevant evidence in the literature to inform the ISA. There are discipline-specific PECOS tools for experimental and epidemiologic studies. The use of PECOS tools is a widely accepted and rapidly growing approach to systematic review in human health risk assessment, and consistent with recommendations by the National Academy of Sciences for improving the design of risk assessment through planning, scoping, and problem formulation to better meet the needs of decision-makers (National Research Council 2009). The PECOS tools serve as guides for several aspects of the ISA process, including the literature search strategy, criteria for the inclusion or exclusion of studies in the ISA, the types of data extracted from studies, and the integration and synthesis of the results.

The health appendices of the ISA will evaluate the scientific literature related to a range of health effects associated with exposures to Pb, including, but not limited to, nervous system, cardiovascular, reproductive, and developmental effects. Building upon the last review, the EPA will continue to review the available epidemiologic and toxicological evidence related to these health endpoints and to the extent data are available, to additional health endpoints. The results

of new studies will be integrated with the previous findings along with any new interpretations of previous findings that the new studies may elicit. The ISA will also integrate previous information on at-risk lifestages and populations with new evidence for existing and possibly newly identified at-risk factors.

For a given health outcome, the ISA will fully integrate findings across the different disciplines to evaluate the strength and consistency of evidence. Integration will also entail using relevant toxicological and epidemiologic studies to assess biological plausibility for findings of observed health effects. Efforts will be directed at identifying the lower levels at which effects are observed and at determining concentration-response relationships with a focus on lower level Pb exposures. Concentration-response relationships also will be evaluated for coherence across the studies. Another area of focus, carried over from the previous review, includes assessment of exposure durations and developmental time periods of exposure that are most strongly associated with health effects. The ISA will also assess the evidence for uncertainties related to these associations and evaluate information on the public health implications related to ambient air Pb exposure.

The scope of the ecological effects portion of the ISA is defined by a scoping framework modeled on PECOS for human health. The Level of Biological Organization, Exposure, Comparison, Endpoint, and Study Design (LECES) tool aids in identifying the relevant evidence in the literature for ecological effects of Pb to inform the ISA. The scope of the ecological effects portion of the ISA takes into consideration studies that examine Pb interactions with biotic and abiotic components of ecosystems. Topics within scope include how biogeochemistry of Pb affects bioavailability in terrestrial, freshwater, and saltwater environments; biological effects of Pb exposure in different environmental media (e.g., soil, sediment, water); subsequent vulnerability of particular organisms, populations, communities, or ecosystems; as well as studies that address key uncertainties and limitations in the evidence identified in the previous review. Relevant concentrations for welfare effects of Pb will take into consideration the range of Pb concentrations in the environment and the available evidence for concentrations at which effects are observed in plants, invertebrates, and vertebrates. Effects observed at or near Pb concentrations measured in ambient soil, sediment and water for which local contamination is not thought to be a primary contributor will be emphasized. Studies at higher concentrations will be considered to the extent that they inform modes of action, exposure-response, or the wide range of sensitivity to Pb across taxa. Areas outside of the scope of the ecological effects appendix include site-specific studies in non-US locations that do not contribute novel insights on Pb biogeochemistry or effects. Studies of laboratory animal models that inform human responses that are relevant for assessment of Pb effects on human health are assessed in the health appendices of the ISA, as scoped using the PECOS tool described above. To the extent

such models are also relevant to biological responses in the natural environment, these studies may be considered in the characterization of ecological effects. Generally, studies on mine tailings, biochar, industrial effluent, sewage, ship breaking, bioremediation of highly contaminated sites, and ingestion of Pb shot, fishing tackle or pellets are not within the scope of the ISA due to high concentration of Pb and lack of a connection to an air-related source or process.

3.3 SPECIFIC SCIENTIFIC QUESTIONS

Specific scientific questions guide the evaluation of new literature that meets the scope described in Section 3. For health and ecological effects, an initial set of questions are considered to evaluate new evidence in the context of causality determinations that were made in the 2013 ISA (see IRP Vol. 1, Section A.4 for more information on the causal framework). In characterizing the current scientific evidence, the Pb ISA will also consider discipline-specific questions on the extent to which the recent literature has identified new limitations and uncertainties and/or addressed limitations and uncertainties identified in prior reviews. The scientific questions specific to this ISA are organized into broad topic areas and presented in the ensuing subsections.

3.3.1 Source to Concentration – Air Quality Atmospheric Science, Fate and Transport

Specific science questions that we plan to address in the ISA related to air quality, atmospheric chemistry, fate, and transport include the following:

<u>Sources, Fate & Transport, Atmospheric Concentrations and Measurements</u>

- Is new information available on sources of Pb to ambient air? For example, what does current evidence indicate regarding impacts of leaded aviation gas on airborne and deposited Pb? What new evidence or methodologies exist regarding differentiation between recently emitted and historical sources of Pb? What new evidence or methodologies exist regarding the differentiation between anthropogenic and natural Pb concentrations?
- Is new evidence available on the distribution of airborne Pb in different particle sizes, including in locations near Pb sources or in the near-road environment? What new evidence is available regarding the use of monitors to characterize Pb in different particle size fractions (e.g., TSP, PM10), and the relationships between them, accurately?
- What new evidence exists regarding the spatial and temporal variability of airborne and deposited Pb concentrations?
- What new measurement and modeling methods, if any, have been developed that improve our understanding and predictive capabilities for Pb multimedia concentrations and distribution?

- What new evidence exists to improve characterization of fate and transport of ambient air Pb, including dispersion, deposition, and resuspension of Pb-containing particles through multiple media? Are there any new modeling techniques that may improve our understanding of these processes? What new studies of the environmental fate and transport of Pb or new evidence on the distribution of ambient air Pb into different media (including indoor dust, soil, sediment, and surface water) are available that might inform our assessment of ecological or human exposures?

3.3.2 Exposure, Toxicokinetics, Biomarkers

Specific science questions related to exposure, toxicokinetics, and biomarkers that we plan to address in the ISA include:

- What new evidence is available on population and/or lifestage variability in Pb biokinetics?
- What new developments are available in biokinetic models that can be used for estimating impacts of multimedia human Pb exposures on internal body burden, generally indicated by blood Pb levels or bone Pb? Is there new evidence, including bioaccessibility studies, to inform our understanding of the response of blood Pb to changes in ambient air Pb and associated exposure pathways?
- What new evidence is available on biological factors (e.g., age, diet, gender, race) that could affect the interpretation of blood Pb and bone Pb concentrations? How and to what extent does previous Pb exposure, including duration (e.g., acute, subchronic, chronic) and pattern (e.g., continuous low, extreme peak), impact blood Pb and bone Pb?
- What new evidence is available on the relationship between air Pb and blood Pb levels and uncertainties in that relationship? What new knowledge exists regarding the characterization of changes in this relationship when accounting for the multiple pathways of Pb exposure and body burden associated with Pb exposure? What does the current evidence indicate regarding variation in this relationship with variation in blood Pb levels or air Pb levels?
- To what extent does new scientific evidence increase our understanding of the contributions of Pb from different sources and exposure pathways to blood Pb levels or to other indicators of Pb body burden (e.g., air-related and other contributions of diet and indoor dust pathways)?
- What new evidence is there regarding the use of different biomarkers to assess Pb exposure (Pb in blood, bone, urine, hair, nails, or teeth)?
- What does the current evidence indicate regarding blood Pb levels in different age groups and how does that relate to those age groups in the past? What does that indicate with regard to the childhood exposures of today's older adults and differences from those of today's young adults?

3.3.3 Health Effects

3.3.3.1 Causality Determinations from the 2013 ISA

The causality determinations in the 2013 ISA, based on the causal framework (see IRP Volume 1) and integration of available evidence from previous and recent studies, were presented with a summary of the available evidence at the end of the sections for each broad health and welfare effect category and in the Integrative Synthesis chapter at the beginning of the document.

In the 2013 ISA, the evidence for human health effects is organized into groups of related endpoints (e.g., cognitive function, externalizing behaviors, neurodegenerative diseases) for which causality determinations were made. There were a total of 33 causality determinations made for related endpoints across 13 broad health effect categories (e.g., nervous system effects, cardiovascular effects, renal effects). The EPA concluded that the findings of epidemiologic and animal toxicological studies collectively provided evidence of a "causal relationship" for Pb exposures and cognitive function in children; externalizing behaviors in children: attention, impulsivity, and hyperactivity; hypertension; coronary heart disease; decreased red blood cell survival and function; altered heme synthesis; development; and male reproductive effects. The full summary of causality determinations for human health effects is presented in Table 3-1.

Table 3-1. Summary of causality determinations from the 2013 ISA organized by health outcome.

Health Outcome	Causality Determination
Nervous System Effects - Children	
Cognitive Function Decrements	Causal Relationship
Externalizing Behaviors: Attention, Impulsivity, and Hyperactivity	Causal Relationship
Externalizing Behaviors: Conduct Disorders in Children and Young Adults	Likely Causal Relationship
Internalizing Behaviors	Likely Causal Relationship
Auditory Function Decrements	Likely Causal Relationship
Visual Function Decrements	Inadequate to Infer a Causal Relationship
Motor Function Decrements	Likely Causal Relationship
Nervous System Effects - Adults	
Cognitive Function Decrements	Likely Causal Relationship
Psychopathological Effects	Likely Causal Relationship
Auditory Function Decrements	Suggestive of a Causal Relationship
Visual Function Decrements	Inadequate to Infer a Causal Relationship
Neurodegenerative Diseases	Inadequate to Infer a Causal Relationship
Cardiovascular Effects	
Hypertension	Causal Relationship

Health Outcome	Causality Determination
Subclinical Atherosclerosis	Suggestive of a Causal Relationship
Coronary Heart Disease	Causal Relationship
Cerebrovascular Disease	Inadequate to Infer a Causal Relationship
Renal Effects	
Reduced Kidney Function	Suggestive of a Causal Relationship
Immune System Effects	
Atopic and Inflammatory Responses	Likely Causal Relationship
Decreased Host Resistance	Likely Causal Relationship
Autoimmunity	Inadequate to Infer a Causal Relationship
Hematological Effects	
Decreased Red Blood Cell Survival and Function	Causal Relationship
Altered Heme Synthesis	Causal Relationship
Reproductive and Developmental Effects	
Development	Causal Relationship
Birth Outcomes	Suggestive of a Causal Relationship
Male Reproductive Function	Causal Relationship
Female Reproductive Function	Suggestive of a Causal Relationship
Effects on the Hepatic System	
Hepatic Effects	Inadequate to Infer a Causal Relationship
Effects on the Gastrointestinal System	
Gastrointestinal Effects	Inadequate to Infer a Causal Relationship
Effects on the Endocrine System	
Endocrine Effects	Inadequate to Infer a Causal Relationship
Effects on Bone and Teeth	
Effects on Bone and Teeth	Likely Causal Relationship
Effects on Ocular Health	
Ocular Effects	Inadequate to Infer a Causal Relationship
Effects on the Respiratory System	
Respiratory	Inadequate to Infer a Causal Relationship
Cancer	
Cancer	Likely Causal Relationship

In the current review, specific science questions related to the causality determinations for health effects of Pb that we plan to address include:

- Does the evidence base from studies published since the 2013 ISA (literature cutoff September 2011) contain new information to support, extend, or call into question the causality determinations made in the 2013 ISA?
- Is there new information to support causality determinations for other endpoints not covered in the 2013 ISA?

- Does new evidence confirm, extend, or call into question prior conclusions on the biological plausibility for specific Pb-related health effects?
- What does the available information indicate with regard to changes in population health status that may be associated with a decrease in Pb exposure that might inform causality determinations?

3.3.3.2 Other Science Questions

In addition to general questions related to the causality determinations, more specific questions on the health effects of Pb, biological plausibility, and areas of uncertainty identified in the previous NAAQS review will also shape the aims of this assessment. Grouped by topic area, some of the other specific scientific questions that the EPA will seek to address in the ISA are as follows.

Health Effects: The ISA will evaluate health effects evidence for a multitude of outcomes from epidemiologic and toxicological studies.

- How do results of recent epidemiologic studies and current or new interpretations of previous findings expand our understanding of the relationship between body burdens of Pb and neurological effects in children and adults, including deficits in IQ, behavior, learning, motor skills, and risk of neurodegenerative diseases? Specifically, do recent studies expand the current understanding of the concentration-response relationships at the lower range of Pb exposures presently relevant to the U.S. population, particularly in young children for whom observed relationships are less likely to be confounded by Pb exposures earlier in childhood?
- How do different body burdens of Pb (e.g., blood, bone) compare in terms of their associations with health outcomes? What do these findings contribute to understanding of about how effects may differ between more recent and cumulative lifetime exposure?
- What new evidence is available on health effects of Pb exposure in older adults (e.g., cardiovascular mortality and neurodegenerative diseases)? What does the current evidence indicate regarding the exposures and blood Pb levels that these cohorts likely experienced through their lifetime, and what does such evidence indicate regarding the potential for different impacts of early-life, current, and cumulative lifetime Pb exposures?
- Does new evidence from the animal toxicology literature on developmental exposures to Pb and adult outcomes inform the understanding of populations and life stages that are susceptible to Pb exposure (e.g., Alzheimer's disease, obesity, behavioral changes)? Within such developmentally sensitive windows, are there epigenetic changes, genetic polymorphism or sex-based differences that increase risk of Pb-related health effects? What does this evidence indicate regarding exposure levels to which such effects are attributable?
- Is there new evidence of associations with biological markers that may provide supporting information on biological plausibility of observed effects?

- What new evidence has become available to help discern health effects of exposure to Pb within mixtures - including mixtures with other toxic metals, other pollutants in ambient air, or other environmental exposures - versus Pb alone (e.g., additive, synergistic, or antagonistic effects)?

Uncertainties: The ISA will evaluate uncertainty in the scientific data, particularly in relation to observed epidemiologic findings and their consistency with toxicological studies in terms of observed effects and biological pathways.

- To what extent are the observed associations between Pb biomarkers and health outcomes attributable to exposure to Pb rather than co-exposures to other toxic metals or environmental contaminants?[7]
- Are seasonal trends evident for Pb concentrations, exposures, or Pb-related health effects?
- To what extent can new epidemiologic studies differentiate the role of recent versus past exposures in Pb-related health effects observed in older children and adults, whose longer exposure histories may complicate the interpretation of Pb biomarker associations with health outcomes?
- Based on the new body of evidence, to what extent do epidemiologic models address uncertainties regarding linearity and/or the discernability of thresholds in the concentration-response relationships for Pb-related health effects? What evidence is newly available on the uncertainties related to other aspects of statistical model specification and how can it be used to assess the influence of these uncertainties on the outcome of epidemiologic studies? What evidence is available from toxicological studies of concentration- or dose-response relationships?

Biological Plausibility: The ISA will evaluate the data examining mechanisms for the health outcomes associated with exposure to Pb.

- To what extent is new evidence available regarding mechanisms for nervous system effects associated with lower blood Pb levels (i.e., <5 μg/dL in young children)?
- To what extent is new evidence available in humans regarding the Pb exposure level, timing, frequency, and duration associated with mechanisms for health effects. Are new animal models available to better characterize biological plausibility at different levels, windows, frequencies, and duration of exposures?
- To what extent is new evidence available regarding biological plausibility at various ages and developmental stages that result in different effects and/or effects at lower exposures? Are new animal models available to better characterize biological plausibility at various lifestages?

[7] Epidemiologic evidence is unlikely to evaluate all potentially correlated metals and contaminants, and the limitations of epidemiologic methods in separating effects of highly correlated exposures or separating the effects of more than two co-exposures in the same model are well-recognized. Thus, coherence with other lines of evidence may strengthen inferences when there are uncertainties in epidemiologic evidence due to confounding by co-exposures.

- What mechanistic evidence is available that would help us understand health effects of exposure to Pb within mixtures versus Pb alone (e.g., additive, synergistic, or antagonistic effects)?

3.3.4 At-Risk Lifestages and Populations and public Health Impact

The NAAQS are intended to protect public health with an adequate margin of safety, including protection for the populations or lifestages potentially at increased risk for Pb-related health effects. Thus, the ISA will evaluate evidence for an array of factors that may contribute to increased risk of Pb-related health effects for various lifestages or populations (e.g., lifestages in early development). The evaluation of recent evidence will build on the conclusions from the 2013 ISA, where application of the at-risk framework[8] to classify evidence demonstrated that there was adequate evidence that children are at increased risk of Pb-related health effects. The 2013 ISA also concluded that there was adequate evidence that a number of other factors contributed to increased risk of Pb-related health effects, including, but not limited to, being of a certain race/ethnicity and poor nutrition. The ISA will evaluate recent evidence that informs the identification of at-risk factors in each of the health appendices. Key considerations in characterizing the evidence include consistency of findings for a factor within a discipline and, where available, coherence of the evidence across disciplines as well as biological plausibility. When evaluating evidence to inform the identification of at-risk lifestages or populations, emphasis will be placed on the health effects for which there is a causal or likely to be a causal relationship with exposure to Pb. Specific questions we plan to address include:

- What new evidence is available to further support, extend, or call into question the at-risk determination made for lifestages or populations in the 2013 ISA?
- What new evidence is available regarding additional lifestages or populations (e.g., pre-existing diseases such as diabetes) potentially at increased risk of a Pb-related health effect?
- Is there new information that identifies a combination of factors (i.e., co-occurring) that can lead to one lifestage or population being at greater risk compared to another?

3.3.5 Ecological Effects

3.3.5.1 Causality Determinations from the 2013 ISA

This ISA will evaluate the recent evidence related to effects of Pb exposures in terrestrial and aquatic organisms. In the 2013 ISA, causality determinations for ecological effects of Pb

[8] In recent reviews, the term "at-risk" has been used to define populations and lifestages potentially at increased risk of an air pollutant-related health effect (e.g., see 2013 Pb ISA and 2020 Ozone ISA; U.S. EPA, 2013; U.S. EPA, 2020). At-risk populations can include those with intrinsic factors that make them more susceptible to pollutant-related effects (e.g., pre-existing disease, genetic characteristics) or that increase pollutant dose (e.g., breathing patterns), and extrinsic factors that could increase pollutant exposures (e.g., personal activity patterns) (U.S. EPA, 2020, pp. IS-50).

were organized by organism category (plants, invertebrates, vertebrates) across three ecosystem types (terrestrial, freshwater, saltwater). There were a total of 51 causality determinations made for related endpoints across 7 broad effect categories (e.g., physiological stress, hematological effects, neurobehavioral effects, survival, growth, reproductive and developmental effects, community and ecosystem effects) (Table 3-2). Overall, freshwater invertebrates were among the most sensitive biota to Pb, whereas there was considerably less evidence for saltwater organisms. The evidence indicated a "causal relationship" between Pb exposure and reproductive effects in terrestrial and freshwater vertebrates and invertebrates, growth effects in terrestrial plants and freshwater invertebrates, and survival in terrestrial and freshwater invertebrates as well as for freshwater vertebrates. Additionally, there were causal relationships between Pb exposure and sub-organismal responses of hematological effects in terrestrial and freshwater vertebrates and markers of physiological stress in plants. The evidence indicated a "likely to be causal relationship" for terrestrial and freshwater community and ecosystem level effects, whereas there was inadequate evidence in saltwater ecosystems. For organism-level response there were "likely to be causal" relationships between Pb exposure and freshwater plant growth, terrestrial invertebrate growth, survival of terrestrial vertebrates and neurobehavioral effects in terrestrial and freshwater vertebrates and invertebrates.

Table 3-2. Summary of causality determinations from the 2013 ISA for the relationship between exposure to Pb and ecological effects.

Level		Effect	Terrestrial[a]	Freshwater[a]	Saltwater[a]
Community- and Ecosystem		Community and Ecosystem Effects	Likely Causal	Likely Causal	Inadequate
Population–Level Endpoints	Organism–Level Responses	Reproductive and Developmental Effects-Plants	Inadequate	Inadequate	Inadequate
		Reproductive and Developmental Effects-Invertebrates	Causal	Causal	Suggestive
		Reproductive and Developmental Effects-Vertebrates	Causal	Causal	Inadequate
		Growth-Plants	Causal	Likely Causal	Inadequate
		Growth-Invertebrates	Likely Causal	Causal	Inadequate
		Growth-Vertebrates	Inadequate	Inadequate	Inadequate
		Survival-Plants	Inadequate	Inadequate	Inadequate
		Survival- Invertebrates	Causal	Causal	Inadequate
		Survival- Vertebrates	Likely Causal	Causal	Inadequate
		Neurobehavioral Effects-Invertebrates	Likely Causal	Likely Causal	Inadequate
		Neurobehavioral Effects-Vertebrates	Likely Causal	Likely Causal	Inadequate
	Sub-organismal Responses	Hematological Effects-Invertebrates	Inadequate	Likely Causal	Suggestive
		Hematological Effects-Vertebrates	Causal	Causal	Inadequate
		Physiological Stress-Plants	Causal	Likely Causal	Inadequate
		Physiological Stress-Invertebrates	Likely Causal	Likely Causal	Suggestive
		Physiological Stress-Vertebrates	Likely Causal	Likely Causal	Inadequate

[a] Based on the weight of evidence for causal determination in Table II of the ISA Preamble. Ecological causal determinations are based on doses or exposures generally within one to two orders of magnitude of the range of Pb currently measured in the environment (Table 2-1 of the 2013 ISA for Pb).

In the current review, specific science questions related to the causality determinations for ecological effects that we plan to address include:

- Does the evidence base from studies published since the 2013 ISA (literature cutoff September 2011) contain new information to support, extend, or call into question the causality determinations made in the 2013 ISA?
- Is there new information to support causality determinations for other endpoints not covered in the 2013 ISA?

The previous review recognized the persistence of Pb in the environment and concluded that the combination of Pb accumulated from past deposition, and much smaller ongoing deposition contributes to total Pb loading in terrestrial and aquatic systems. In both terrestrial and aquatic biota gradients in response are observed in which effects increase with increasing concentration of Pb. Causality determinations for ecological effects of Pb in the 2013 ISA used biological scale as an organizing principle to summarize effects on vegetation and invertebrates and vertebrates in terrestrial, freshwater, and saltwater environments (Table 3-2). For effects that occur at the sub-organism scale emphasis was placed on studies that also report effects experimentally linked to higher levels of biological organization (i.e., from the cellular and subcellular level to the individual organism up to ecosystem level effects). Some studies in the previous review on reproduction, growth, and survival endpoints in sensitive freshwater invertebrates reported effects from a few controlled studies at concentrations at or near Pb concentrations within the range of Pb detected in environmental media over the past several decades. Generally, in the previous review, there were fewer studies available for saltwater organisms compared to terrestrial and freshwater biota, and therefore the evidence was often inadequate to relate Pb exposure to specific endpoints in coastal environments. Available studies on ecological community and ecosystem-level effects were usually from contaminated areas where Pb concentrations are much higher than typically encountered in areas away from point sources and highly impacted sites.

3.3.5.2 Other Science Questions

In the 2013 ISA, a substantial portion of the evidence for effects of Pb on biota were from laboratory exposures under controlled conditions. In natural environments, abiotic and biotic modifying factors affect Pb bioavailability and toxicity, and there are uncertainties associated with generalizing effects observed in controlled studies to effects at higher levels of biological organization. Furthermore, biological effects vary with species, lifestage, duration of exposure, and form of Pb. An additional uncertainty in the last review was the lack of studies specifically examining a connection between air concentration of Pb and ecosystem exposure. The current review of the literature will consider if there is evidence that addresses any of these uncertainties as well as any new information on effects of Pb on ecological receptors. Discussions will include

additional information on modifying factors if available, and consideration of the extent to which evidence from experimental studies that used high Pb exposures informs interpretation of effects at the generally lower exposures that are currently widespread in the environment. Some scientific questions that the EPA will seek to address in the ISA follow, grouped by broad ecosystem type:

Terrestrial Ecosystem Effects:

- What new information is available about the nature of the effects of Pb on terrestrial ecosystems? Is there new evidence of effects associated with Pb concentrations resulting from current atmospheric deposition, especially that relevant to the current NAAQS?
- Are there newly identified ecological endpoints or processes affected by Pb in terrestrial biota? Is there new information available for establishing specific exposure levels at which terrestrial ecological receptors are expected to experience effects?
- Are there new empirical data or modeling results that would improve our understanding of Pb bioavailability and mechanisms of exposure to terrestrial organisms?
- Is there new information on modifying factors in terrestrial environments that attenuate or enhance Pb toxicity to biota?
- What new evidence exists to improve characterization of Pb from atmospheric sources to terrestrial biota? Is there indication that terrestrial ecosystems have responded to temporal and/or spatial trends in atmospheric Pb deposition?
- Does any of the new evidence contribute to a better understanding of the nature and magnitude of the potential effects of Pb on terrestrial ecosystem services?

Aquatic Ecosystem Effects:

- What new information is available about the nature of the effects of Pb on aquatic ecosystems? Is there new evidence of effects associated with Pb concentrations resulting from current atmospheric deposition, especially that relevant to the current NAAQS?
- Are there newly identified ecological endpoints or processes affected by Pb in freshwater or saltwater biota? Is there new information available for establishing specific exposure levels at which aquatic ecological receptors are expected to experience effects?
- Are there new empirical data or modeling results that would improve our understanding of Pb bioavailability and mechanisms of exposure to aquatic organisms?
- Is there new information on modifying factors in aquatic environments that attenuate or enhance Pb toxicity to biota?
- What new evidence exists to improve characterization of Pb from atmospheric sources to aquatic biota? Is there indication that aquatic ecosystems have responded to temporal and/or spatial trends in atmospheric Pb deposition?
- Does any of the new evidence contribute to a better understanding of the nature and magnitude of the potential effects of Pb on aquatic ecosystem services?

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Appendix

Draft Organization of Pb ISA

Preface

Executive Summary

Integrative Synthesis

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