

## APPENDIX A. ATSDR MINIMAL RISK LEVEL WORKSHEETS

MRLs are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified route and duration of exposure. MRLs are based on noncancer health effects only; cancer effects are not considered. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels.

MRLs are derived for hazardous substances using the NOAEL/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1–14 days), intermediate (15–364 days), and chronic ( $\geq 365$  days) durations and for the oral and inhalation routes of exposure. Currently, MRLs for the dermal route of exposure are not derived because ATSDR has not yet identified a method suitable for this route of exposure. MRLs are generally based on the most sensitive substance-induced endpoint considered to be of relevance to humans. Serious health effects (such as irreparable damage to the liver or kidneys, or birth defects) are not used as a basis for establishing MRLs. Exposure to a level above the MRL does not mean that adverse health effects will occur.

MRLs are intended only to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites that are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as 100-fold below levels that have been shown to be nontoxic in laboratory animals.

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Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology and Human Health Sciences, expert panel peer reviews, and agency-wide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published MRLs. For additional information regarding MRLs, please contact the Division of Toxicology and Human Health Sciences, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road NE, Mailstop S102-1, Atlanta, Georgia 30329-4027.

The literature evaluating the health effects of Pb is enormous, and includes an extensive database in humans, including children. Effects are diverse and exposure to Pb is associated with toxicity to every organ system. For the most studied endpoints (neurological, renal, cardiovascular, hematological, immunological, reproductive, and developmental), effects occur at the lowest PbBs studied ( $\leq 5 \mu\text{g/dL}$ ). Exposure thresholds for effects on specific organ systems have not been identified (i.e., no safe level has been identified). Cognitive deficits in children occurring at the lowest PbBs ( $\leq 5 \mu\text{g/dL}$ ) are the best substantiated effects. However, because the lowest PbBs are associated with serious adverse effects (e.g., declining cognitive function in children), MRLs for Pb have not been derived.

## APPENDIX B. LITERATURE SEARCH FRAMEWORK FOR LEAD

The objective of the toxicological profile is to evaluate the potential for human exposure and the potential health hazards associated with inhalation, oral, or dermal/ocular exposure to Pb.

### B.1 LITERATURE SEARCH AND SCREEN

A literature search and screen were conducted to identify studies examining health effects, toxicokinetics, mechanisms of action, susceptible populations, biomarkers, chemical interactions, physical and chemical properties, production, use, environmental fate, environmental releases, and environmental and biological monitoring data for Pb. ATSDR primarily focused on peer-reviewed articles without publication date or language restrictions. Non-peer-reviewed studies that were considered relevant to the assessment of the health effects of Pb have undergone peer review by at least three ATSDR-selected experts who have been screened for conflict of interest. The inclusion criteria used to identify relevant studies examining the health effects of Pb are presented in Table B-1.

**Table B-1. Inclusion Criteria for the Literature Search and Screen**

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Health Effects
Species
Human
Laboratory mammals
Route of exposure
Inhalation
Oral
Dermal (or ocular)
Parenteral (these studies will be considered supporting data)
Health outcome
Death
Systemic effects
Body weight effects
Respiratory effects
Cardiovascular effects
Gastrointestinal effects
Hematological effects
Musculoskeletal effects
Hepatic effects
Renal effects
Dermal effects
Ocular effects
Endocrine effects
Immunological effects
Neurological effects
Reproductive effects
Developmental effects
Other noncancer effects

**Table B-1. Inclusion Criteria for the Literature Search and Screen**

Cancer
Toxicokinetics
Absorption
Distribution
Metabolism
Excretion
PBPK models
Biomarkers
Biomarkers of exposure
Biomarkers of effect
Interactions with other chemicals
Potential for human exposure
Releases to the environment
Air
Water
Soil
Environmental fate
Transport and partitioning
Transformation and degradation
Environmental monitoring
Air
Water
Sediment and soil
Other media
Biomonitoring
General populations
Occupation populations

### B.1.1 Literature Search

The current literature search was intended to update the draft toxicological profile for Pb released for public comment in 2019; thus, the literature search was restricted to studies published between February 2015 and September 2019. The following main databases were searched in September 2019:

- PubMed
- National Library of Medicine's TOXLINE
- Scientific and Technical Information Network's TOXCENTER

The search strategy used the chemical names, Chemical Abstracts Service (CAS) numbers, synonyms, Medical Subject Headings (MeSH) headings, and keywords for Pb. The query strings used for the literature search are presented in Table B-2.

The search was augmented by searching the Toxic Substances Control Act Test Submissions (TSCATS), NTP website, and National Institute of Health Research Portfolio Online Reporting Tools Expenditures

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and Results (NIH RePORTER) databases using the queries presented in Table B-3. Additional databases were searched in the creation of various tables and figures, such as the TRI Explorer, the Substance Priority List (SPL) resource page, and other items as needed. Regulations applicable to Pb were identified by searching international and U.S. agency websites and documents.

Review articles were identified and used for the purpose of providing background information and identifying additional references. ATSDR also identified reports from the grey literature, which included unpublished research reports, technical reports from government agencies, conference proceedings and abstracts, and theses and dissertations.

**Table B-2. Database Query Strings**

Database	search date	Query string
<b>PubMed</b>		
09/2019		<p>(((((10031-22-8[rn] OR 10099-74-8[rn] OR 10101-63-0[rn] OR 11119-70-3[rn] OR 12709-98-7[rn] OR 1309-60-0[rn] OR 1314-41-6[rn] OR 1314-87-0[rn] OR 1317-36-8[rn] [ 13424-46-9[rn] OR 13814-96-5[rn] OR 15245-44-0[rn] OR 16040-38-3[rn] OR 39377-56-5[rn] OR 598-63-0[rn] OR 7439-92-1[rn] OR 7446-14-2[rn] OR 7446-27-7[rn] OR 7758-95-4[rn] OR 7758-97-6[rn] OR 78-00-2[rn] OR 301-04-2[rn] ) AND (((("Lead/toxicity"[mh] OR "Lead/adverse effects"[mh] OR "Lead/poisoning"[mh] OR "Lead/pharmacokinetics"[mh] OR ("Lead"[mh] AND ("environmental exposure"[mh] OR ci[sh])) OR ("Lead"[mh] AND toxicokinetics[mh:noexp]) OR ("Lead/blood"[mh] OR "Lead/cerebrospinal fluid"[mh] OR "Lead/urine"[mh]) OR ("Lead"[mh] AND ("endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine disruptors"[mh])) OR ("Lead"[mh] AND ("computational biology"[mh] OR "medical informatics"[mh] OR genomics[mh] OR genome[mh] OR proteomics[mh] OR proteome[mh] OR metabolomics[mh] OR metabolome[mh] OR genes[mh] OR "gene expression"[mh] OR phenotype[mh] OR genetics[mh] OR genotype[mh] OR transcriptome[mh] OR ("systems biology"[mh] AND ("environmental exposure"[mh] OR "epidemiological monitoring"[mh] OR analysis[sh])) OR "transcription, genetic "[mh] OR "reverse transcription"[mh] OR "transcriptional activation"[mh] OR "transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, messenger"[mh] OR "RNA, transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "reverse transcriptase polymerase chain reaction"[mh] OR "base sequence"[mh] OR "trans-activators"[mh] OR "gene expression profiling"[mh])) OR ("Lead/antagonists and inhibitors"[mh]) OR ("Lead/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Lead"[majr] AND cancer[sb]) OR ("Lead/pharmacology"[majr])) AND (2016/02/01 : 3000[mhda] OR 2016/02/01 : 3000[crdt] OR 2016/02/01 : 3000[edat] OR 2015/02/01 : 3000[dp])) OR ("lead poisoning"[mh] AND (2016/02/01 : 3000[mhda] OR 2016/02/01 : 3000[crdt] OR 2016/02/01 : 3000[edat] OR 2015/02/01 : 3000[dp])) OR (((("Tetraethyl Lead/toxicity"[mh] OR "Tetraethyl Lead/adverse effects"[mh] OR "Tetraethyl Lead/poisoning"[mh] OR "Tetraethyl Lead/pharmacokinetics"[mh]) OR ("Tetraethyl Lead"[mh] AND ("environmental exposure"[mh] OR ci[sh])) OR ("Tetraethyl Lead"[mh] AND toxicokinetics[mh:noexp]) OR ("Tetraethyl Lead/blood"[mh] OR "Tetraethyl Lead/cerebrospinal fluid"[mh] OR "Tetraethyl Lead/urine"[mh]) OR ("Tetraethyl Lead"[mh] AND ("endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine disruptors"[mh])) OR ("Tetraethyl Lead"[mh] AND ("computational biology"[mh] OR "medical informatics"[mh] OR genomics[mh] OR genome[mh] OR proteomics[mh] OR proteome[mh] OR metabolomics[mh] OR metabolome[mh] OR genes[mh] OR "gene expression"[mh] OR phenotype[mh] OR genetics[mh] OR genotype[mh] OR transcriptome[mh] OR ("systems biology"[mh] AND ("environmental exposure"[mh] OR "epidemiological monitoring"[mh] OR analysis[sh])) OR "transcription, genetic "[mh] OR "reverse transcription"[mh] OR</p>

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**Table B-2. Database Query Strings**

Database	search date	Query string
		<p>"transcriptional activation"[mh] OR "transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, messenger"[mh] OR "RNA, transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "reverse transcriptase polymerase chain reaction"[mh] OR "base sequence"[mh] OR "trans-activators"[mh] OR "gene expression profiling"[mh])) OR ("Tetraethyl Lead/antagonists and inhibitors"[mh]) OR ("Tetraethyl Lead/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Tetraethyl Lead"[majr] AND cancer[sb]) OR ("Tetraethyl Lead/pharmacology"[majr]) AND (2016/02/01 : 3000[mhda] OR 2016/02/01 : 3000[crdt] OR 2016/02/01 : 3000[edat] OR 2015/02/01 : 3000[dp])) OR ((301-04-2[rn] AND ("Organometallic Compounds/toxicity"[mh] OR "Organometallic Compounds/adverse effects"[mh] OR "Organometallic Compounds/poisoning"[mh] OR "Organometallic Compounds/pharmacokinetics"[mh]) OR ("Organometallic Compounds"[mh] AND ("environmental exposure"[mh] OR ci[sh])) OR ("Organometallic Compounds"[mh] AND toxicokinetics[mh:noexp]) OR ("Organometallic Compounds/blood"[mh] OR "Organometallic Compounds/cerebrospinal fluid"[mh] OR "Organometallic Compounds/urine"[mh]) OR ("Organometallic Compounds"[mh] AND ("endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine disruptors"[mh])) OR ("Organometallic Compounds"[mh] AND ("computational biology"[mh] OR "medical informatics"[mh] OR genomics[mh] OR genome[mh] OR proteomics[mh] OR proteome[mh] OR metabolomics[mh] OR metabolome[mh] OR genes[mh] OR "gene expression"[mh] OR phenotype[mh] OR genetics[mh] OR genotype[mh] OR transcriptome[mh] OR ("systems biology"[mh] AND ("environmental exposure"[mh] OR "epidemiological monitoring"[mh] OR analysis[sh])) OR "transcription, genetic "[mh] OR "reverse transcription"[mh] OR "transcriptional activation"[mh] OR "transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, messenger"[mh] OR "RNA, transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "reverse transcriptase polymerase chain reaction"[mh] OR "base sequence"[mh] OR "trans-activators"[mh] OR "gene expression profiling"[mh])) OR ("Organometallic Compounds/antagonists and inhibitors"[mh] OR ("Organometallic Compounds/metabolism"[mh] AND ("humans"[mh] OR "animals"[mh])) OR ("Organometallic Compounds"[majr] AND cancer[sb]) OR ("Organometallic Compounds/pharmacology"[majr])) AND (2016/02/01 : 3000[mhda] OR 2016/02/01 : 3000[crdt] OR 2016/02/01 : 3000[edat] OR 2015/02/01 : 3000[dp])) OR (((("1,3-Benzenediol, 2,4,6-trinitro-, lead(2+) salt"[tw] OR "Borate(1-), tetrafluoro-, lead (2+) "[tw] OR "Borate(1-), tetrafluoro-, lead(2+) "[tw] OR "Chromic acid lead salt with lead molybdate"[tw] OR "Chromic acid, lead and molybdenum salt"[tw] OR "Chromium lead molybdenum oxide"[tw] OR "Lead (II) iodide"[tw] OR "Lead 2,4,6-trinitro-m-phenylene dioxide"[tw] OR "Lead bis(tetrafluoroborate)"[tw] OR "Lead borofluoride"[tw] OR "Lead boron fluoride"[tw] OR "Lead Brown"[tw] OR "Lead chromate molybdate"[tw] OR "lead diiodide"[tw] OR "Lead dioxide"[tw] OR "Lead fluoborate"[tw] OR "Lead fluoroborate"[tw] OR "Lead iodide"[tw] OR "Lead molybdate chromate"[tw] OR "Lead molybdenum chromate"[tw] OR "Lead oxide"[tw] OR "Lead peroxide"[tw] OR "Lead styphnate"[tw] OR "Lead superoxide"[tw] OR "Lead tetrafluoroborate"[tw] OR "Lead trichinate"[tw] OR "Lead trinitroresorcinate"[tw] OR "Lead(II) iodide"[tw] OR "Lead(II) styphnate"[tw] OR "Lead(II) tetrafluoroborate"[tw] OR "Lead(IV) oxide"[tw] OR "Lead-molybdenum chromate"[tw] OR "Molybdenum-lead chromate"[tw] OR "Plumbic oxide"[tw] OR "Plumbous iodide"[tw] OR "Plumbum jodatum"[tw] OR "Resorcinol, 2,4,6-trinitro-, lead(2+) salt"[tw] OR "Thiolead A"[tw] OR "Tricinat"[tw]) AND (to[sh] OR po[sh] OR ae[sh] OR pk[sh] OR ai[sh] OR ci[sh] OR bl[sh] OR cf[sh] OR ur[sh] OR "pharmacology"[sh:noexp] OR "environmental exposure"[mh] OR "endocrine system"[mh] OR "hormones, hormone substitutes, and hormone antagonists"[mh] OR "endocrine</p>

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**Table B-2. Database Query Strings**

Database search date	Query string
	<p> disruptors[mh] OR "Computational biology"[mh] OR "Medical Informatics"[mh] OR Genomics[mh] OR Genome[mh] OR Proteomics[mh] OR Proteome[mh] OR Metabolomics[mh] OR Metabolome[mh] OR Genes[mh] OR "Gene expression"[mh] OR Phenotype[mh] OR genetics[mh] OR genotype[mh] OR Transcriptome[mh] OR ("Systems Biology"[mh] AND ("Environmental Exposure"[mh] OR "Epidemiological Monitoring"[mh] OR analysis[sh])) OR "Transcription, Genetic "[mh] OR "Reverse transcription"[mh] OR "Transcriptional activation"[mh] OR "Transcription factors"[mh] OR ("biosynthesis"[sh] AND (RNA[mh] OR DNA[mh])) OR "RNA, Messenger"[mh] OR "RNA, Transfer"[mh] OR "peptide biosynthesis"[mh] OR "protein biosynthesis"[mh] OR "Reverse Transcriptase Polymerase Chain Reaction"[mh] OR "Base Sequence"[mh] OR "Trans-activators"[mh] OR "Gene Expression Profiling"[mh] OR cancer[sb] OR (me[sh] AND ("humans"[mh] OR "animals"[mh]))) AND (2016/02/01 : 3000[mhda] OR 2016/02/01 : 3000[crdt] OR 2016/02/01 : 3000[edat] OR 2015/02/01 : 3000[dp])) OR (("Plumbism"[tw] OR "saturnism"[tw] OR "colica pictorum"[tw] OR "Devon colic"[tw] OR "painter's colic"[tw]) NOT "lead poisoning"[mh]) OR (((("1,3-Benzenediol, 2,4,6-trinitro-, lead(2+) salt (1:1)"[tw] OR "Acetic acid lead(2+) salt"[tw] OR "Acetic acid, lead salt"[tw] OR "Acetic acid, lead(2+) salt"[tw] OR "Acetic acid, lead(2+) salt"[tw] OR "Anglislite"[tw] OR "Azarcon"[tw] OR "Borate(1-), tetrafluoro-, lead (2+)"[tw] OR "Borate(1-), tetrafluoro-, lead(2+) (2:1)"[tw] OR "C.I. Pigment Metal 4"[tw] OR "C.I. Pigment Yellow 46"[tw] OR "CARBONIC ACID, LEAD SALT (1:1)"[tw] OR "Carbonic acid, lead salt (2+) (1:1)"[tw] OR "Carbonic acid, lead(2+) salt"[tw] OR "Cerussite"[tw] OR "Cerussite"[tw] OR "Chrome Orange"[tw] OR "Chrome Yellow"[tw] OR "Chromic acid (H<sub>2</sub>CrO<sub>4</sub>), lead(2+) salt (1:1)"[tw] OR "Chromic acid lead salt "[tw] OR "CHROMIC ACID, LEAD (2+) SALT (1:1)"[tw] OR "Chromic Acid, Lead (II) Salt (1:1)"[tw] OR "Chromic acid, lead and molybdenum salt"[tw] OR "Chromic acid, lead salt"[tw] OR "Chromic acid, lead(2+) salt (1:1)"[tw] OR "Chromium lead molybdenum oxide"[tw] OR "Chromium lead oxide"[tw] OR "CI pigment metal 4"[tw] OR "CI Pigment Yellow 46"[tw] OR "Collodial lead phosphate"[tw] OR "Dibasic lead acetate"[tw] OR "Dibasic lead carbonate"[tw] OR "Dibasic lead sulfate"[tw] OR "Entan"[tw] OR "Fast White"[tw] OR "Flowsperse R 12"[tw] OR "Freemans White Lead"[tw] OR "Galena"[tw] OR "Glover"[tw] OR "Gold Satinobre"[tw] OR "Heuconin 5"[tw] OR "Lead (II) carbonate"[tw] OR "Lead (II) chloride"[tw] OR "Lead (II) chromate"[tw] OR "Lead (II) iodide"[tw] OR "Lead (II) nitrate"[tw] OR "Lead (II) oxide"[tw] OR "Lead (II) sulfate"[tw] OR "Lead (II) sulfide"[tw] OR "Lead (II, IV) oxide"[tw] OR "Lead (IV) oxide "[tw] OR "Lead 2,4,6-trinitro-m-phenylene dioxide"[tw] OR "Lead acetate"[tw] OR "Lead azide"[tw] OR "Lead bis(tetrafluoroborate)"[tw] OR "Lead borofluoride"[tw] OR "Lead boron fluoride"[tw] OR "Lead Bottoms"[tw] OR "Lead bromide"[tw] OR "Lead brown"[tw] OR "Lead carbonate"[tw] OR "Lead chloride"[tw] OR "Lead chromate"[tw] OR "Lead chromate(VI)"[tw] OR "Lead chromium oxide (PbCrO<sub>4</sub>)"[tw] OR "Lead di(acetate)"[tw] OR "Lead diacetate"[tw] OR "Lead diazide"[tw] OR "Lead dibasic acetate"[tw] OR "Lead dibromide"[tw] OR "Lead dichloride"[tw] OR "Lead diiodide"[tw] OR "Lead dinitrate"[tw] OR "Lead dioxide"[tw] OR "Lead element"[tw] OR "Lead flake"[tw] OR "Lead fluoborate"[tw] OR "Lead fluoroborate"[tw] OR "Lead iodide"[tw] OR "Lead metal"[tw] OR "Lead molybdate chromate"[tw] OR "Lead molybdenum chromate"[tw] OR "Lead monoxide"[tw] OR "Lead monosulfate"[tw] OR "Lead monosulfide"[tw] OR "Lead monoxide"[tw] OR "Lead nitrate"[tw] OR "Lead orthophosphate"[tw] OR "Lead orthoplumbate"[tw] OR "Lead oxide"[tw] OR "Lead peroxide"[tw] OR "Lead phosphate"[tw] OR "Lead protoxide"[tw] OR "Lead S 2"[tw] OR "Lead S<sub>2</sub>"[tw] OR "Lead styphnate"[tw] OR "Lead sulfate"[tw] OR "Lead sulfide"[tw] OR "Lead sulphate"[tw] OR "Lead sulphide"[tw] OR "Lead superoxide"[tw] OR "Lead tetraethide"[tw] OR "Lead tetraethyl"[tw] OR "Lead tetrafluoroborate"[tw] OR "Lead tetraoxide"[tw] OR "Lead tetroxide"[tw] OR "Lead triciniate"[tw] OR "Lead </p>

**Table B-2. Database Query Strings**

Database search date	Query string
	<p>trinitroresorcinatetw OR "Lead(+2) sulfatetw OR "Lead(2+) acetatetw OR "Lead(2+) azidetw OR "Lead(2+) bis(nitratetw OR "Lead(2+) bromidetw OR "Lead(2+) carbonatetw OR "Lead(2+) chloridetw OR "Lead(2+) nitratetw OR "Lead(2+) oxidetw OR "Lead(2+) phosphatetw OR "Lead(2+) phosphate (Pb3(PO4)2)tw OR "Lead(2+) salt carbamic acid (1:1) tw OR "Lead(2+) sulfatetw OR "Lead(2+) sulfidetw OR "Lead(II) acetatetw OR "Lead(II) azidetw OR "Lead(II) bromidetw OR "Lead(II) carbonatetw OR "Lead(II) chloridetw OR "Lead(II) chromatetw OR "Lead(II) dinitratetw OR "Lead(II) iodidetw OR "Lead(II) nitratetw OR "Lead(II) oxidetw OR "Lead(II) phosphatetw OR "Lead(II) phosphate (3:2)tw OR "Lead(II) styphnatetw OR "Lead(II) sulfatetw OR "Lead(II) sulfidetw OR "Lead(II) tetrafluoroboratetw OR "Lead(IV) oxidetw OR "Lead, elementaltw OR "Lead, inorganictw OR "Lead, tetraethyltw OR "Lead, tetraethyl-tw OR "Lead-molybdenum chromatetw OR "Litharge"tw OR "Massicot"tw OR "Massicotite"tw OR "Mennige"tw OR "Milk White"tw OR "mine orangetw OR "Mineral Orangetw OR "Mineral red"tw OR "minio anaranjado"tw OR "Minium"tw OR "Molybdenum-lead chromatetw OR "Mulhouse Whitetw OR "Nitric acid lead(2+) salt"tw OR "Nitric acid, lead(2+) salt"tw OR "Orange lead"tw OR "Orangemennige"tw OR "Paris Red"tw OR "PbSO4"tw OR "Perlex paste 500"tw OR "Perlex paste 600A"tw OR "Phoenicochroite"tw OR "Phosphoric acid, lead salt"tw OR "Phosphoric acid, lead(2+) salt (2:3)tw OR "Pigment Red 105"tw OR "Pigment White 3"tw OR "Pigment Yellow 34"tw OR "Pigment Yellow 46"tw OR "Plumbane"tw OR "Plumbi"tw OR "Plumbic oxide"tw OR "Plumboplumbic oxide"tw OR "Plumbous"tw OR "Plumbum"tw OR "Red lead"tw OR "Resorcinol, 2,4,6-trinitro-, lead(2+) salt (1:1)tw OR "Rough lead bullion"tw OR "Royal Yellow 6000"tw OR "Salt of saturn"tw OR "Sandix"tw OR "Saturn red"tw OR "Sugar of lead"tw OR "Sulfuric acid, lead(2+) salt"tw OR "Tetra Ethylene Lead"tw OR "Tetra(methylethyl)lead"tw OR "Tetraethyl lead"tw OR "Tetraethyl plumbane"tw OR "Tetraethyllead"tw OR "Tetraethyllead, liquid"tw OR "tetraethylplomb"tw OR "Tetraethylplombane"tw OR "Tetraethylplumbane"tw OR "tetraetilplomo"tw OR "Thiolead A"tw OR "Tricinat"tw OR "Trilead bis(orthophosphate)"tw OR "Trilead phosphate"tw OR "Trilead tetraoxide"tw OR "Trilead tetroxide"tw OR "Unichem PBA"tw OR "Yellow lead ocher"tw) NOT medline[sbj] AND (2016/02/01 : 3000[crdt] OR 2016/02/01 : 3000[edat] OR 2015/02/01 : 3000[dpj])) OR (((("Lead"[ti] NOT "lead to"[ti]) OR "Pb"[ti] OR "PbS"[ti] OR "PbO"[ti]) NOT medline[sbj] AND (2016/02/01 : 3000[crdt] OR 2016/02/01 : 3000[edat] OR 2015/02/01 : 3000[dpj]))</p>
<b>Toxline</b> 09/2019	<p>Date limit: 2015 to present: (10031-22-8[rn] OR 10099-74-8[rn] OR 10101-63-0[rn] OR 11119-70-3[rn] OR 12709-98-7[rn] OR 1309-60-0[rn] OR 1314-41-6[rn] OR 1314-87-0[rn] OR 1317-36-8[rn] OR 13424-46-9[rn] OR 13814-96-5[rn] OR 15245-44-0[rn] OR 16040-38-3[rn] OR 39377-56-5[rn] OR 598-63-0[rn] OR 7439-92-1[rn] OR 7446-14-2[rn] OR 7446-27-7[rn] OR 7758-95-4[rn] OR 7758-97-6[rn] OR 78-00-2[rn]) AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTc [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] ) ("1,3-Benzenediol, 2,4,6-trinitro-, lead(2+) salt (1:1)" OR "Acetic acid lead(2+) salt" OR "Acetic acid, lead salt" OR "Acetic acid, lead(2+) salt" OR "Acetic acid, lead(2+) salt" OR "Anglislite" OR "Azarcon" OR "Borate(1-), tetrafluoro-, lead (2+)" OR "Borate(1-), tetrafluoro-, lead(2+) (2:1)" OR "C.I. Pigment Metal 4" OR "C.I. Pigment Yellow 46" OR "CARBONIC ACID, LEAD SALT (1:1)" OR "Carbonic acid, lead salt (2+) (1:1)" AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM</p>



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**Table B-2. Database Query Strings**

Database	search date	Query string
		[org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Carbonic acid, lead(2+) salt" OR "Cerussite" OR "Cerussite" OR "Chrome Orange" OR "Chrome Yellow" OR "Chromic acid (H <sub>2</sub> CrO <sub>4</sub> ), lead(2+) salt (1:1)" OR "Chromic acid lead salt " OR "CHROMIC ACID, LEAD (2+) SALT (1:1)" OR "Chromic Acid, Lead (II) Salt (1:1)" OR "Chromic acid, lead and molybdenum salt" OR "Chromic acid, lead salt" OR "Chromic acid, lead(2+) salt (1:1)" OR "Chromium lead molybdenum oxide") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Chromium lead oxide" OR "CI pigment metal 4" OR "CI Pigment Yellow 46" OR "Colloidal lead phosphate" OR "Dibasic lead acetate" OR "Dibasic lead carbonate" OR "Dibasic lead sulfate" OR "Entan" OR "Fast White" OR "Flowperse R 12" OR "Freemans White Lead" OR "Galena" OR "Glover" OR "Gold Satinobre" OR "Heuconin 5" OR "Lead (II) carbonate" OR "Lead (II) chloride" OR "Lead (II) chromate" OR "Lead (II) iodide" OR "Lead (II) nitrate" OR "Lead (II) oxide" OR "Lead (II) sulfate" OR "Lead (II) sulfide") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Lead (II,IV) oxide" OR "Lead (IV) oxide " OR "Lead 2,4,6-trinitro-m-phenylene dioxide" OR "Lead acetate" OR "Lead azide" OR "Lead bis(tetrafluoroborate)" OR "Lead borofluoride" OR "Lead boron fluoride" OR "Lead Bottoms" OR "Lead bromide" OR "Lead brown" OR "Lead carbonate" OR "Lead chloride" OR "Lead chromate" OR "Lead chromate(VI)" OR "Lead chromium oxide (PbCrO <sub>4</sub> )" OR "Lead di(acetate)") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Lead diacetate" OR "Lead diazide" OR "Lead dibasic acetate" OR "Lead dibromide" OR "Lead dichloride" OR "Lead diiodide" OR "Lead dinitrate" OR "Lead dioxide" OR "Lead element" OR "Lead flake" OR "Lead fluoborate" OR "Lead fluoroborate" OR "Lead iodide" OR "Lead metal" OR "Lead molybdate chromate" OR "Lead molybdenum chromate" OR "Lead monoxide" OR "Lead monosulfate" OR "Lead monosulfide") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Lead monoxide" OR "Lead nitrate" OR "Lead orthophosphate" OR "Lead orthoplumbate" OR "Lead oxide" OR "Lead peroxide" OR "Lead phosphate" OR "Lead protoxide" OR "Lead S 2" OR "Lead S2" OR "Lead styphnate" OR "Lead sulfate" OR "Lead sulfide" OR "Lead sulphate" OR "Lead sulphide" OR "Lead superoxide" OR "Lead tetraethide" OR "Lead tetraethyl" OR "Lead tetrafluoroborate" OR "Lead tetraoxide") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Lead tetroxide" OR "Lead tricinate" OR "Lead trinitroresorcinat" OR "Lead(+2) sulfate" OR "Lead(2+) acetate" OR "Lead(2+) azide" OR "Lead(2+) bis(nitrate)" OR "Lead(2+) bromide" OR "Lead(2+) carbonate" OR "Lead(2+) chloride" OR "Lead(2+) nitrate" OR "Lead(2+) oxide" OR "Lead(2+) phosphate" OR "Lead(2+) phosphate (Pb <sub>3</sub> (PO <sub>4</sub> ) <sub>2</sub> )" OR "Lead(2+) salt carbamic acid (1:1) " OR "Lead(2+) sulfate") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP

**Table B-2. Database Query Strings**

Database	search date	Query string
		[org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Lead(2+) sulfide" OR "Lead(II) acetate" OR "Lead(II) azide" OR "Lead(II) bromide" OR "Lead(II) carbonate" OR "Lead(II) chloride" OR "Lead(II) chromate" OR "Lead(II) dinitrate" OR "Lead(II) iodide" OR "Lead(II) nitrate" OR "Lead(II) oxide" OR "Lead(II) phosphate" OR "Lead(II) phosphate (3:2)" OR "Lead(II) styphnate" OR "Lead(II) sulfate" OR "Lead(II) sulfide" OR "Lead(II) tetrafluoroborate" OR "Lead(IV) oxide") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Lead, elemental" OR "Lead, inorganic" OR "Lead, tetraethyl" OR "Lead, tetraethyl-" OR "Lead-molybdenum chromate" OR "Litharge" OR "Massicot" OR "Massicotite" OR "Mennige" OR "Milk White" OR "mine orange" OR "Mineral Orange" OR "Mineral red" OR "minio anaranjado" OR "Minium" OR "Molybdenum-lead chromate" OR "Mulhouse White" OR "Nitric acid lead(2+) salt" OR "Nitric acid, lead(2+) salt") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Orange lead" OR "Orangemennige" OR "Paris Red" OR "PbSO4" OR "Perlex paste 500" OR "Perlex paste 600A" OR "Phoenicochroite" OR "Phosphoric acid, lead salt" OR "Phosphoric acid, lead(2+) salt (2:3)" OR "Pigment Red 105" OR "Pigment White 3" OR "Pigment Yellow 34" OR "Pigment Yellow 46" OR "Plumbane" OR "Plumbi" OR "Plumbic oxide" OR "Plumboplumbic oxide" OR "Plumbous" OR "Plumbum") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Red lead" OR "Resorcinol, 2,4,6-trinitro-, lead(2+) salt (1:1)" OR "Rough lead bullion" OR "Royal Yellow 6000" OR "Salt of saturn" OR "Sandix" OR "Saturn red" OR "Sugar of lead" OR "Sulfuric acid, lead(2+) salt" OR "Tetra Ethylene Lead" OR "Tetra(methylethyl)lead" OR "Tetraethyl lead" OR "Tetraethyl plumbane" OR "Tetraethyllead" OR "Tetraethyllead, liquid" OR "tetraethylplomb") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		("Tetraethylplumbane" OR "Tetraethylplumbane" OR "tetraetilplomo" OR "Thiolead A" OR "Tricinat" OR "Trilead bis(orthophosphate)" OR "Trilead phosphate" OR "Trilead tetraoxide" OR "Trilead tetroxide" OR "Unichem PBA" OR "Yellow lead ocher") AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		Term searched as exact words: "lead" AND ( ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR HEEP [org] OR HMTTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org] )
		Date limit: 2013 to present: "Plumbism" OR "saturnism" OR "colica pictorum" OR "Devon colic" OR "painter's colic"
<b>Toxcenter</b>		
09/2019	L1	8918 SEA 10031-22-8 OR 10099-74-8 OR 10101-63-0 OR 11119-70-3 OR

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**Table B-2. Database Query Strings**

Database search date	Query string
	12709-98-7 OR 1309-60-0 OR 1314-41-6 OR 1314-87-0 OR 1317-36-8 OR 13424-46-9
L2	239150 SEA 13814-96-5 OR 15245-44-0 OR 16040-38-3 OR 301-04-2 OR 39377-56-5 OR 598-63-0 OR 7439-92-1 OR 7446-14-2 OR 7446-27-7 OR 7758-95-4 OR 7758-97-6 OR 78-00-2
L3	244612 SEA L1 OR L2
L4	244408 SEA L3 NOT TSCATS/FS
L5	225905 SEA L4 NOT PATENT/DT
L6	26519 SEA L5 AND ED>=20160201 ACT TOXQUERY/Q -----
L7	QUE (CHRONIC OR IMMUNOTOX? OR NEUROTOX? OR TOXICOKIN? OR BIOMARKER? OR NEUROLOG?)
L8	QUE (PHARMACOKIN? OR SUBCHRONIC OR PBPK OR EPIDEMIOLOGY/ST,CT, IT)
L9	QUE (ACUTE OR SUBACUTE OR LD50# OR LD(W)50 OR LC50# OR LC(W)50)
L10	QUE (TOXICITY OR ADVERSE OR POISONING)/ST,CT,IT
L11	QUE (INHAL? OR PULMON? OR NASAL? OR LUNG? OR RESPIR?)
L12	QUE ((OCCUPATION? OR WORKPLACE? OR WORKER?) AND EXPOS?)
L13	QUE (ORAL OR ORALLY OR INGEST? OR GAVAGE? OR DIET OR DIETS OR DIETARY OR DRINKING(W)WATER?)
L14	QUE (MAXIMUM AND CONCENTRATION? AND (ALLOWABLE OR PERMISSIBLE))
L15	QUE (ABORT? OR ABNORMALIT? OR EMBRYO? OR CLEFT? OR FETUS?)
L16	QUE (FOETUS? OR FETAL? OR FOETAL? OR FERTIL? OR MALFORM? OR OVUM?)
L17	QUE (OVA OR OVARY OR PLACENTA? OR PREGNAN? OR PRENATAL?)
L18	QUE (PERINATAL? OR POSTNATAL? OR REPRODUC? OR STERIL? OR TERATOGEN?)
L19	QUE (SPERM OR SPERMAC? OR SPERMAG? OR SPERMATI? OR SPERMAS? OR SPERMATOB? OR SPERMATOC? OR SPERMATOG?)
L20	QUE (SPERMATOI? OR SPERMATOL? OR SPERMATOR? OR SPERMATOX? OR SPERMATOZ? OR SPERMATU? OR SPERMI? OR SPERMO?)
L21	QUE (NEONAT? OR NEWBORN? OR DEVELOPMENT OR DEVELOPMENTAL?)
L22	QUE (ENDOCRIN? AND DISRUPT?)
L23	QUE (ZYGOTE? OR CHILD OR CHILDREN OR ADOLESCEN? OR INFANT?)
L24	QUE (WEAN? OR OFFSPRING OR AGE(W)FACTOR?)
L25	QUE (DERMAL? OR DERMIS OR SKIN OR EPIDERM? OR CUTANEOUS?)
L26	QUE (CARCINO? OR COCARCINO? OR CANCER? OR PRECANCER? OR NEOPLAS?)
L27	QUE (TUMOR? OR TUMOUR? OR ONCOGEN? OR LYMPHOMA? OR CARCINOM?)
L28	QUE (GENETOX? OR GENOTOX? OR MUTAGEN? OR GENETIC(W)TOXIC?)
L29	QUE (NEPHROTOX? OR HEPATOTOX?)
L30	QUE (ENDOCRIN? OR ESTROGEN? OR ANDROGEN? OR HORMON?)
L31	QUE (OCCUPATION? OR WORKER? OR WORKPLACE? OR EPIDEM?)
L32	QUE L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31
L33	QUE (RAT OR RATS OR MOUSE OR MICE OR GUINEA(W)PIG? OR MURIDAE OR DOG OR DOGS OR RABBIT? OR HAMSTER? OR PIG OR PIGS OR SWINE OR PORCINE OR MONKEY? OR MACAQUE?)
L34	QUE (MARMOSSET? OR FERRET? OR GERBIL? OR RODENT? OR LAGOMORPHA OR BABOON? OR CANINE OR CAT OR CATS OR FELINE OR MURINE)
L35	QUE L32 OR L33 OR L34
L36	QUE (HUMAN OR HUMANS OR HOMINIDAE OR MAMMALS OR MAMMAL? OR

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**Table B-2. Database Query Strings**

Database search date	Query string
L37	PRIMATES OR PRIMATE?) QUE L35 OR L36 -----
L38	14067 SEA L6 AND L37
L39	2663 SEA L38 AND MEDLINE/FS
L40	4980 SEA L38 AND BIOSIS/FS
L41	6411 SEA L38 AND CAPLUS/FS
L42	13 SEA L38 NOT (L39 OR L40 OR L41)
L43	11438 DUP REM L39 L40 L42 L41 (2629 DUPLICATES REMOVED) ANSWERS '1-11438' FROM FILE TOXCENTER
L*** DEL	2663 S L38 AND MEDLINE/FS
L*** DEL	2663 S L38 AND MEDLINE/FS
L44	2663 SEA L43
L*** DEL	4980 S L38 AND BIOSIS/FS
L*** DEL	4980 S L38 AND BIOSIS/FS
L45	3952 SEA L43
L*** DEL	6411 S L38 AND CAPLUS/FS
L*** DEL	6411 S L38 AND CAPLUS/FS
L46	4810 SEA L43
L*** DEL	13 S L38 NOT (L39 OR L40 OR L41)
L*** DEL	13 S L38 NOT (L39 OR L40 OR L41)
L47	13 SEA L43
L48	8775 SEA (L44 OR L45 OR L46 OR L47) NOT MEDLINE/FS SAVE TEMP L48 LEAD/A

**Table B-3. Strategies to Augment the Literature Search**

Source	Query and number screened when available
<b>TSCATS via ChemView</b>	
09/2019	Compounds searched: 10031-22-8; 10099-74-8; 10101-63-0; 11119-70-3; 12709-98-7; 1309-60-0; 1314-41-6; 1314-87-0; 1317-36-8; 13424-46-9; 13814-96-5; 15245-44-0; 16040-38-3; 301-04-2; 39377-56-5; 598-63-0; 7439-92-1; 7446-14-2; 7446-27-7; 7758-95-4; 7758-97-6; 78-00-2
<b>NTP</b>	
09/2019	NTP Site Search ( <a href="http://ntpsearch.niehs.nih.gov/home">http://ntpsearch.niehs.nih.gov/home</a> ), date limit 2015 to present: "10031-22-8" "10099-74-8" "10101-63-0" "11119-70-3" "12709-98-7" "1309-60-0" "1314-41-6" "1314-87-0" "1317-36-8" "13424-46-9" "13814-96-5" "15245-44-0" "16040-38-3" "301-04-2" "39377-56-5" "598-63-0" "7439-92-1" "7446-14-2" "7446-27-7" "7758-95-4" "7758-97-6" "78-00-2"  Limited to content types reports & publications; systematic reviews; ROC profiles, reviews, or candidates; or testing status, date limit 2015 to present: "lead"
<b>Regulations.gov</b>	
10/2019	Compounds searched: 10031-22-8; 10099-74-8; 10101-63-0; 11119-70-3; 12709-98-7; 1309-60-0; 1314-41-6; 1314-87-0; 1317-36-8; 13424-46-9; 13814-

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**Table B-3. Strategies to Augment the Literature Search**

Source	Query and number screened when available
	96-5; 15245-44-0; 16040-38-3; 301-04-2; 39377-56-5; 598-63-0; 7439-92-1; 7446-14-2; 7446-27-7; 7758-95-4; 7758-97-6; 78-00-2
<b>NIH RePORTER</b>	<p data-bbox="488 428 1414 485">01/2020 Search in: Projects AdminIC: All, Fiscal Year: Active Projects Text Search (Advanced):</p> <p data-bbox="488 489 1425 1493">"1,3-Benzenediol, 2,4,6-trinitro-, lead" OR "Acetic acid lead " OR "Acetic acid, lead salt" OR "Acetic acid, lead " OR "Acetic acid, lead " OR "Anglislite" OR "Azarcon" OR "Borate(1-), tetrafluoro-, lead" OR "Borate(1-), tetrafluoro-, lead" OR "C.I. Pigment Metal 4" OR "C.I. Pigment Yellow 46" OR "CARBONIC ACID, LEAD SALT" OR "Carbonic acid, lead salt" OR "Carbonic acid, lead" OR "Cerussite" OR "Cerussite" OR "Chrome Orange" OR "Chrome Yellow" OR "Chromic acid (H2CrO4), lead" OR "Chromic acid lead salt " OR "CHROMIC ACID, LEAD" OR "Chromic Acid, Lead (II) Salt" OR "Chromic acid, lead and molybdenum salt" OR "Chromic acid, lead salt" OR "Chromic acid, lead" OR "Chromium lead molybdenum oxide" OR "Chromium lead oxide" OR "CI pigment metal 4" OR "CI Pigment Yellow 46" OR "Collodial lead phosphate" OR "Dibasic lead acetate" OR "Dibasic lead carbonate" OR "Dibasic lead sulfate" OR "Entan" OR "Fast White" OR "Flowsperse R 12" OR "Freemans White Lead" OR "Galena" OR "Glover" OR "Gold Satinobre" OR "Heuconin 5" OR "Lead (II) carbonate" OR "Lead (II) chloride" OR "Lead (II) chromate" OR "Lead (II) iodide" OR "Lead (II) nitrate" OR "Lead (II) oxide" OR "Lead (II) sulfate" OR "Lead (II) sulfide" OR "Lead (II, IV) oxide" OR "Lead (IV) oxide " OR "Lead 2,4,6-trinitro-m-phenylene dioxide" OR "Lead acetate" OR "Lead azide" OR "Lead bis(tetrafluoroborate)" OR "Lead borofluoride" OR "Lead boron fluoride" OR "Lead Bottoms" OR "Lead bromide" OR "Lead brown" OR "Lead carbonate" OR "Lead chloride" OR "Lead chromate" OR "Lead chromate(VI)" OR "Lead chromium oxide (PbCrO4)" OR "Lead di(acetate)" OR "Lead diacetate" OR "Lead diazide" OR "Lead dibasic acetate" OR "Lead dibromide" OR "Lead dichloride" OR "Lead diiodide" OR "Lead dinitrate" OR "Lead dioxide" OR "Lead element" OR "Lead flake" OR "Lead fluoborate" OR "Lead fluoroborate" OR "Lead iodide" OR "Lead metal" OR "Lead molybdate chromate" OR "Lead molybdenum chromate" OR "Lead monooxide" OR "Lead monosulfate" OR "Lead monosulfide" OR "Lead monoxide" OR "Lead nitrate" OR "Lead orthophosphate" OR "Lead orthoplumbate" OR "Lead oxide" OR "Lead peroxide" OR "Lead phosphate" OR "Lead protoxide" OR "Lead S 2" OR "Lead S2" OR "Lead styphnate" OR "Lead sulfate" OR "Lead sulfide" OR "Lead sulphate" OR "Lead sulphide" OR "Lead superoxide" OR "Lead tetraethide" OR "Lead tetraethyl"</p> <p data-bbox="488 1497 1425 1894">"Lead tetrafluoroborate" OR "Lead tetraoxide" OR "Lead tetroxide" OR "Lead tricinate" OR "Lead trinitroresorcinate" OR "Lead(II) acetate" OR "Lead(II) azide" OR "Lead(II) bromide" OR "Lead(II) carbonate" OR "Lead(II) chloride" OR "Lead(II) chromate" OR "Lead(II) dinitrate" OR "Lead(II) iodide" OR "Lead(II) nitrate" OR "Lead(II) oxide" OR "Lead(II) phosphate" OR "Lead(II) phosphate" OR "Lead(II) styphnate" OR "Lead(II) sulfate" OR "Lead(II) sulfide" OR "Lead(II) tetrafluoroborate" OR "Lead(IV) oxide" OR "Lead, elemental" OR "Lead, inorganic" OR "Lead, tetraethyl" OR "Lead, tetraethyl-" OR "Lead-molybdenum chromate" OR "Litharge" OR "Massicot" OR "Massicotite" OR "Mennige" OR "Milk White" OR "mine orange" OR "Mineral Orange" OR "Mineral red" OR "minio anaranjado" OR "Minium" OR "Molybdenum-lead chromate" OR "Mulhouse White" OR "Nitric acid lead" OR "Nitric acid, lead" OR "Orange lead" OR "Orangemennige" OR "Paris Red" OR "PbSO4" OR "Perlex</p>

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**Table B-3. Strategies to Augment the Literature Search**

Source	Query and number screened when available
	<p>paste 500" OR "Perlex paste 600A" OR "Phoenicochroite" OR "Phosphoric acid, lead salt" OR "Phosphoric acid, lead" OR "Pigment Red 105" OR "Pigment White 3" OR "Pigment Yellow 34" OR "Pigment Yellow 46" OR "Plumbane" OR "Plumbi" OR "Plumbic oxide" OR "Plumboplumbic oxide" OR "Plumbous" OR "Plumbum" OR "Red lead" OR "Resorcinol, 2,4,6-trinitro-, lead" OR "Rough lead bullion" OR "Royal Yellow 6000" OR "Salt of saturn" OR "Sandix" OR "Saturn red" OR "Sugar of lead" OR "Sulfuric acid, lead" OR "Tetra Ethylene Lead" OR "Tetra(methylethyl)lead" OR "Tetraethyl lead" OR "Tetraethyl plumbane" OR "Tetraethyllead" OR "Tetraethyllead, liquid" OR "tetraethylplomb" OR "Tetraethylplombane" OR "Tetraethylplumbane" OR "tetraetilplomo" OR "Thiolead A" OR "Tricinat" OR "Trilead bis(orthophosphate)" OR "Trilead phosphate" OR "Trilead tetraoxide" OR "Trilead tetroxide" OR "Unichem PBA" OR "Yellow lead ocher" OR "Lead(2) sulfate" OR "Lead(2) acetate" OR "Lead(2) azide" OR "Lead(2) bis(nitrate)" OR "Lead(2) bromide" OR "Lead(2) carbonate" OR "Lead(2) chloride" OR "Lead(2) nitrate" OR "Lead(2) oxide" OR "Lead(2) phosphate" OR "Lead(2) phosphate (Pb3(PO4)2)" OR "Lead(2) salt carbamic acid" OR "Lead(2) sulfate" OR "Lead(2) sulfide" OR "lead poisoning" OR "Plumbism" OR "saturnism" OR "colica pictorum" OR "Devon colic" OR "painter's colic"</p> <p>"blood lead"</p> <p>Search in: Projects Limit to: Project Title, AdminIC: All, Fiscal Year: Active Projects Text Search (Advanced): "lead" not ("lead academic" or "lead optimization")</p>
<b>Other</b>	Identified throughout the assessment process

The 2019 results were:

- Number of records identified from PubMed, TOXLINE, and TOXCENTER (after duplicate removal): 15,240
- Number of records identified from other strategies: 107
- Total number of records to undergo literature screening: 15,347

### B.1.2 Literature Screening

A two-step process was used to screen the literature search to identify relevant studies on Pb:

- Title and abstract screen
- Full text screen

**Title and Abstract Screen.** Within the reference library, titles and abstracts were screened manually for relevance. Studies that were considered relevant (see Table B-1 for inclusion criteria) were moved to the second step of the literature screening process. Studies were excluded when the title and abstract clearly indicated that the study was not relevant to the toxicological profile.

- Number of titles and abstracts screened: 388
- Number of studies considered relevant and moved to the next step: 388

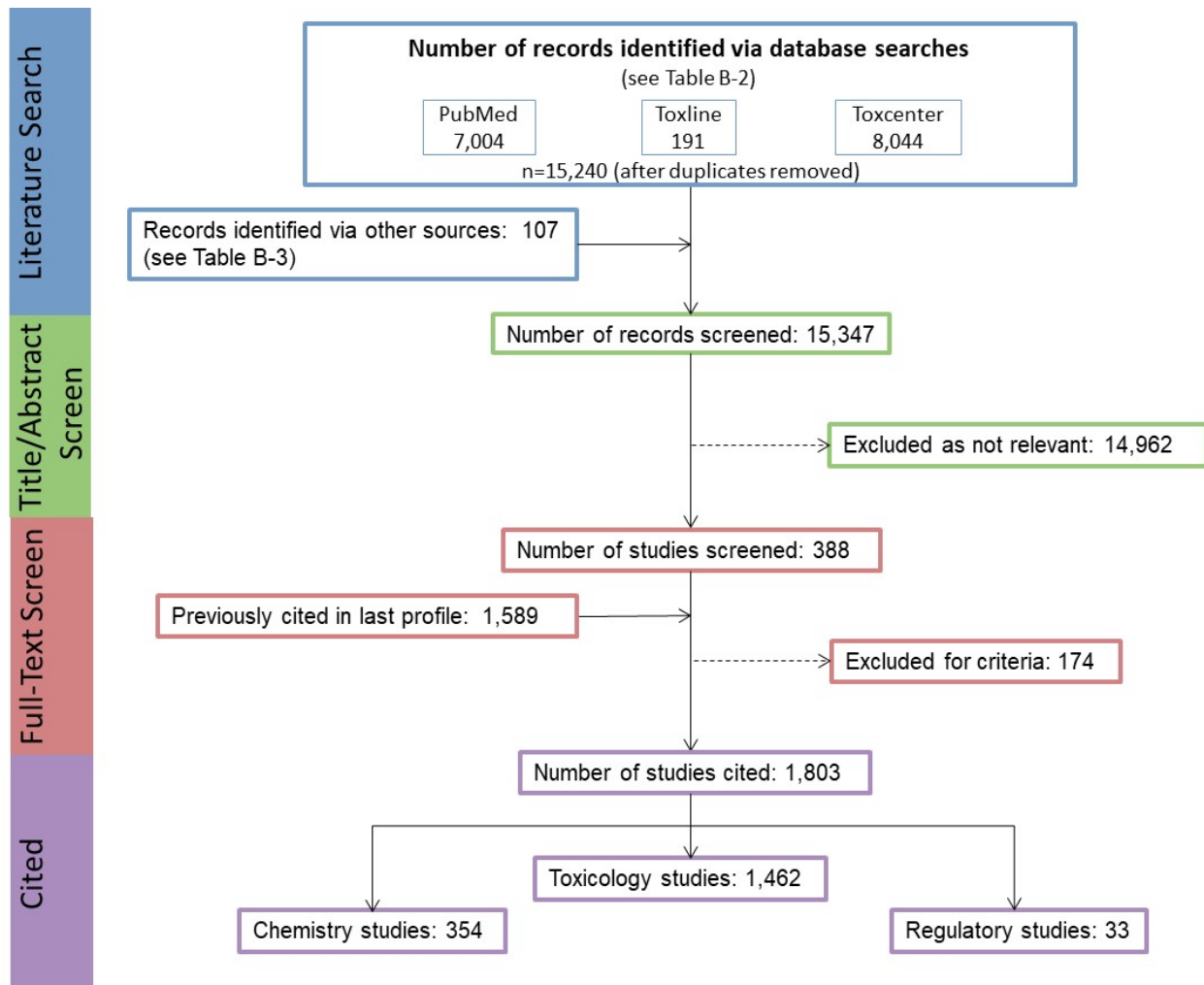
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**Full Text Screen.** The second step in the literature screening process was a full text review of individual studies considered relevant in the title and abstract screen step. Each study was reviewed to determine whether it was relevant for inclusion in the toxicological profile.

- Number of studies undergoing full text review: 388
- Number of studies cited in the pre-public draft of the toxicological profile: 1,589
- Total number of studies cited in the profile: 1,803

A summary of the results of the literature search and screening is presented in Figure B-1.

**Figure B-1. September 2019 Literature Search Results and Screen for Lead (Pb)**



## APPENDIX C. INGESTION OF LEAD DEBRIS

The main focus of this ATSDR Toxicological Profile for Lead is on health effects of chronic low-level environmental exposures. The profile also provides information on the clinical presentation of acute Pb toxicity, which occurs when large amounts of Pb are ingested. In children, this often occurs through ingestion of paint chips containing Pb, Pb-contaminated soils, or other non-solid forms of Pb. Ingestion of solid forms of Pb (Pb debris) is a unique exposure scenario in which there is accidental or purposeful ingestion of visible debris containing Pb. This exposure may be acute (debris is expelled or removed from the body soon after ingestion) or chronic (Pb debris is retained within the body, leading to continued elevation in PbB). There are several sources of Pb debris, including Pb shot or other debris found at firing or artillery ranges, or Pb shot found in wild game meats. The information presented below reviews toxicokinetics and adverse health effects of ingested Pb debris. Information regarding the chemistry, fate, and transport of Pb debris is reviewed in Chapter 5. It should also be noted that in addition to ingestion of Pb debris, retained Pb shot or shrapnel, especially in military personnel, could contribute to elevated PbB (Gerhardsson et al. 2002; McQuirter et al. 2004); this possibility should be considered in individuals as appropriate.

**Overview.** No controlled studies in humans have evaluated bioavailability or toxicity of ingested Pb debris (e.g., Pb shot and other Pb-containing debris from artillery or shooting ranges). Available information is anecdotal, obtained from case reports. Thus, data are not sufficient to determine the bioavailability of ingested Pb debris or to develop dose-response relationships for toxicity. Case reports of acute exposures from ingestion of Pb debris are summarized in Table C-1; these reports demonstrate the following:

- PbB rises rapidly (within hours to a few days) following ingestion of Pb debris.
- The clinical presentation of toxicity following ingestion of Pb debris is the same as that observed for acute Pb poisoning from ingestion of other forms of Pb (see Section 2.2).
- Severity of toxicity of ingested Pb debris will depend upon how much Pb is absorbed (e.g., toxicity is related to PbB; see Section 2.2).
- The onset of toxicity can be rapid (within hours to a few days).
- Following removal of Pb debris from the body, PbBs decrease; however, applying clinical protocols for chelation therapy results in a more rapid decrease in PbB.
- Ingested Pb debris can be retained in the appendix of some individuals and continue to contribute to elevated PbB.



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**Table C-1. Selected Case Studies of Ingestion of Solid Lead (Pb) Debris or Pb Retained in Gunshot Wounds**

Reference and exposure	Blood lead concentration (PbB) (µg/dL)	Effects	Treatment
<p><b>Banner et al. 2012</b></p> <p>A 15-year-old boy ingested a “handful” of Pb shot. He was admitted to the hospital for treatment 14 days after exposure.</p>	<ul style="list-style-type: none"> <li>• Post-ingestion               <ul style="list-style-type: none"> <li>○ 8 days: 54</li> <li>○ 14 days: 41</li> </ul> </li> <li>• Post-treatment (2 weeks): &lt;5</li> </ul>	<ul style="list-style-type: none"> <li>• Most Pb was located in the appendix (14 days post-ingestion)</li> <li>• Abdominal pain</li> <li>• Elevated free erythrocyte protoporphyrin</li> </ul>	<ul style="list-style-type: none"> <li>• Whole bowel irrigation</li> <li>• Appendectomy</li> <li>• Chelation</li> </ul>
<p><b>CDC 2006</b></p> <p>A 4-year-old boy with previously diagnosed microcephaly and mental delays ingested a metallic charm containing Pb. Time from exposure to first medical visit was not reported.</p>	At death: 180	<ul style="list-style-type: none"> <li>• Charm was retained in the stomach (was not removed)</li> <li>• Intractable vomiting</li> <li>• Cerebral edema</li> <li>• Seizures</li> <li>• Death</li> </ul>	Supportive therapy
<p><b>Clifton et al. 2002</b></p> <p>A 21-month-old girl ingested Pb BB pellets. She was taken to the hospital approximately 6 hours post-ingestion.</p>	<ul style="list-style-type: none"> <li>• Pre-ingestion (routine): 12</li> <li>• Post-ingestion (6 hours): 47</li> <li>• Post-removal of pellets: 25</li> <li>• Post-treatment (10 days): 16</li> </ul>	<ul style="list-style-type: none"> <li>• Hyperactivity</li> <li>• No signs of neurological or gastrointestinal toxicity</li> </ul>	<ul style="list-style-type: none"> <li>• Bowel irrigation</li> <li>• Colonoscopy for removal of pellets</li> <li>• Chelation</li> </ul>
<p><b>Cox and Pesola 2005</b></p> <p>A 73-year-old woman ingested Pb shot in game over decades.</p>	Not reported	<ul style="list-style-type: none"> <li>• Pb shot accumulated in the appendix</li> <li>• No information on adverse health effects was reported</li> </ul>	Not reported
<p><b>Durlach et al. 1986</b></p> <p>A 30-year-old man ingested Pb shot in game regularly over an unspecified period of time.</p>	<ul style="list-style-type: none"> <li>• At initial examination: 67.4</li> <li>• Post-treatment               <ul style="list-style-type: none"> <li>○ 10 days: 52.2</li> <li>○ 13 days: 24.5</li> <li>○ 1 month: 36.8</li> <li>○ 1.5 months: 31.6</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Pb shot accumulated in the appendix</li> <li>• Acute abdominal pain</li> </ul>	<ul style="list-style-type: none"> <li>• Bowel irritation</li> <li>• Chelation</li> <li>• Appendectomy</li> </ul>

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**Table C-1. Selected Case Studies of Ingestion of Solid Lead (Pb) Debris or Pb Retained in Gunshot Wounds**

Reference and exposure	Blood lead concentration (PbB) (µg/dL)	Effects	Treatment
<p><b>Fergusson et al. 1997</b></p> <p>A 4-year-old girl ingested a Pb fishing sinker. She was evaluated in the emergency room within 1 hour of ingestion.</p>	<ul style="list-style-type: none"> <li>Day of ingestion: 4</li> <li>Day after ingestion: 16</li> </ul>	No signs of toxicity observed	Endoscopy
<p><b>Gerhardsson et al. 2002</b></p> <p>A man in his "late 40s" had retained Pb shot following a gunshot wound to the shoulder. Reconstructive surgery occurred 54 days post-accident. Some, but not all, of the Pb shot was removed during surgery.</p>	<p>Approximate (data presented graphically), time after accident:</p> <ul style="list-style-type: none"> <li>25 days: 28</li> <li>50 days: 41</li> <li>54 days (day of surgery): 55</li> <li>~60 days: 31</li> <li>75 days: 48</li> <li>200 days: 36</li> <li>375 days: 30</li> </ul>	<ul style="list-style-type: none"> <li>No signs of toxicity observed</li> <li>Not all of the Pb shot could be removed during surgery</li> </ul>	Surgical removal of Pb pellets
<p><b>Guillard et al. 2006</b></p> <p>A 2-year-old boy ingested toy money made from pure metallic Pb.</p>	<p>Time post-ingestion</p> <ul style="list-style-type: none"> <li>1 day: 31.3</li> <li>8 days: 61.1</li> <li>1 month: 30.0</li> <li>4 months: 24.9</li> <li>10 months: 9.9</li> </ul>	<ul style="list-style-type: none"> <li>Development of microcytic anemia and increased blood zinc protoporphyrin</li> <li>No signs of toxicity observed</li> </ul>	<ul style="list-style-type: none"> <li>Removal of object</li> <li>Chelation (8 days post-ingestion)</li> </ul>
<p><b>Gustavsson and Gerhardsson 2005</b></p> <p>A 45-year-old woman with elevated PbB was found to have Pb shot in her intestine from ingestion of game. The Pb shot was spontaneously eliminated. Time from ingestion was estimated to be sometime between 1993 and 2001.</p>	<p>Time of assessment:</p> <ul style="list-style-type: none"> <li>January 2002: 55.0</li> <li>April 2003 (2 months post-elimination): 34.5</li> <li>November 2003: 7.2</li> </ul>	<ul style="list-style-type: none"> <li>Malaise and fatigue</li> <li>"Diffuse gastrointestinal symptoms"</li> </ul>	No treatment (object was spontaneously eliminated)

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**Table C-1. Selected Case Studies of Ingestion of Solid Lead (Pb) Debris or Pb Retained in Gunshot Wounds**

Reference and exposure	Blood lead concentration (PbB) (µg/dL)	Effects	Treatment
<b>Hatten et al. 2013</b>	Case 1	Case 1	Case 1
<ul style="list-style-type: none"> <li>Case 1: A 15-year-old boy ingested rifle cartridges approximately 1 month prior to evaluation.</li> </ul>	<ul style="list-style-type: none"> <li>Initial assessment: 146</li> <li>19 days post-treatment: 53</li> <li>3 months post-treatment: 38</li> </ul>	<ul style="list-style-type: none"> <li>Decreased activity level</li> <li>Vomiting, diarrhea, anorexia</li> <li>Hyperactive patellar and brachioradialis reflexes</li> </ul>	<ul style="list-style-type: none"> <li>Cartridges removed by endoscopy</li> <li>Chelation</li> </ul>
<ul style="list-style-type: none"> <li>Case 2: A 65-year-old woman ingested several handfuls of bullets.</li> </ul>	Case 2: Days after ingestion <ul style="list-style-type: none"> <li>Day 1: 9.7</li> <li>Day 2: 25.7</li> <li>Day 3: 40.5</li> <li>Day 60: 17.2</li> </ul>	Case 2 <ul style="list-style-type: none"> <li>No signs of toxicity were observed</li> </ul>	Case 2 <ul style="list-style-type: none"> <li>Endoscopy</li> </ul>
<b>Larsen and Blanton 2000</b>	Not reported	<ul style="list-style-type: none"> <li>Abdominal pain and anorexia</li> </ul>	Appendectomy
A 9-year-old boy ingested Pb shot in game; the Pb shot was retained in the appendix.			
<b>Lyons and Filston 1994</b>	<ul style="list-style-type: none"> <li>Peak (time of assessment not reported): 23</li> <li>Prior to surgery (1.5 months after ingestion): 12</li> </ul>	<ul style="list-style-type: none"> <li>Abdominal discomfort, nausea, vomiting, diarrhea</li> <li>Headache</li> </ul>	Appendectomy
A 4-year-old boy ingested Pb shot, which was lodged in his appendix.			
<b>Madsen et al. 1988</b>	Range: 4.6–18.2	Not reported	Not reported
Seven patients with Pb shot retained in the appendix.			
<b>McKinney and McKinney 2000</b>	Time after ingestion <ul style="list-style-type: none"> <li>13 hours: 57</li> <li>36 hours: 79</li> </ul> After treatment: <ul style="list-style-type: none"> <li>14 days: 14.3</li> <li>6 months: 25</li> </ul>	<ul style="list-style-type: none"> <li>Vomiting and abdominal pain</li> <li>Decreased blood hemoglobin and hematocrit</li> <li>“Mild” speech and language delays noted post-treatment</li> </ul>	<ul style="list-style-type: none"> <li>Whole bowel irrigation</li> <li>Chelation</li> </ul>
A 5.5-year-old girl ingested several Pb pellets.			

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**Table C-1. Selected Case Studies of Ingestion of Solid Lead (Pb) Debris or Pb Retained in Gunshot Wounds**

Reference and exposure	Blood lead concentration (PbB) (µg/dL)	Effects	Treatment
<p><b>McNutt et al. 2001</b></p> <p>A 45-year-old male ingested 206 Pb bullets. Medical evaluation occurred 5 days after ingestion. Bullets were spontaneously eliminated over 4–47 days after first medical evaluation.</p>	<p>Time after ingestion:</p> <ul style="list-style-type: none"> <li>• 5 days: 391</li> <li>• 10 days: 171</li> <li>• 25 days: 41</li> <li>• 6 weeks: 24</li> </ul>	<ul style="list-style-type: none"> <li>• Abdominal pain and gastrointestinal bleeding</li> <li>• Anemia</li> </ul>	<p>Chelation started at initial medical visit</p>
<p><b>McQuirter et al. 2004</b></p> <p>Subjects (n=451) 1-year following gunshot wound with retained bullets.</p>	<ul style="list-style-type: none"> <li>• PbB at time after injury: 1.9</li> <li>• % with PbB ≥10 (days after injury) <ul style="list-style-type: none"> <li>○ 0 days: 2.1</li> <li>○ 3 days: 7.6</li> <li>○ 18 days: 25.1</li> <li>○ 3 months: 38.1</li> <li>○ 6 months: 28.5</li> <li>○ 12 months: 15.8</li> </ul> </li> </ul>	<p>Not reported</p>	<p>Not reported</p>
<p><b>CDC 2004a</b></p> <p>A 4-year-old boy ingested a Pb medallion.</p>	<ul style="list-style-type: none"> <li>• 2–3 weeks after ingestion: 123</li> <li>• After treatment: 57</li> </ul>	<ul style="list-style-type: none"> <li>• Abdominal pain, vomiting, diarrhea</li> <li>• Normocytic anemia, elevated protoporphyrin</li> </ul>	<ul style="list-style-type: none"> <li>• Endoscopy</li> <li>• Chelation</li> </ul>
<p><b>Mowad et al. 1998</b></p> <p>An 8-year-old boy ingested several Pb fishing sinkers. Medical assessment was within 1 days of ingestion.</p>	<p>Time after ingestion:</p> <ul style="list-style-type: none"> <li>• 1 day: 53</li> <li>• 6 days: 45 (start of chelation)</li> <li>• 1 month: 3</li> </ul>	<p>No signs of toxicity observed</p>	<ul style="list-style-type: none"> <li>• Bowel irrigation</li> <li>• Colonoscopy</li> <li>• Chelation</li> </ul>
<p><b>Rosenberg and Haynes 2019</b></p> <p>A 3-year-old ingested Pb pellets.</p>	<p>Time after ingestion:</p> <ul style="list-style-type: none"> <li>• 7 days: 27</li> <li>• Post-surgical removal: 14</li> </ul>	<p>Not reported</p>	<p>Laparoscopic removal of pellets</p>

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**Table C-1. Selected Case Studies of Ingestion of Solid Lead (Pb) Debris or Pb Retained in Gunshot Wounds**

Reference and exposure	Blood lead concentration (PbB) (µg/dL)	Effects	Treatment
<b>Rozier and Liebelt 2019</b> A 2-year-old boy, a 10-year-old boy, and a 16-year old girl ingested Pb pellets.	2-year-old boy, PbB measurement: <ul style="list-style-type: none"> <li>Day 0: 65</li> <li>5 days post-chelation: 25.2</li> </ul> 10-year-old boy, PbB measurement: <ul style="list-style-type: none"> <li>3 days post-ingestion: 70</li> <li>7 months post-chelation: 9.5</li> </ul> 16-year old girl, PbB measurement: <ul style="list-style-type: none"> <li>9 days post-ingestion: 53</li> <li>13 days post-treatment: 3</li> <li>5 weeks post-treatment: 13</li> </ul>	2-year-old boy: asymptomatic  10-year-old boy: not reported  16-year old girl: <ul style="list-style-type: none"> <li>abdominal pain</li> <li>shortness of breath</li> </ul>	2-year-old boy <ul style="list-style-type: none"> <li>Bowel irrigation</li> <li>Chelation</li> </ul> 10-year-old boy <ul style="list-style-type: none"> <li>Bowel irrigation</li> <li>Chelation</li> </ul> 16-year old girl <ul style="list-style-type: none"> <li>Bowel irrigation</li> <li>Chelation</li> <li>Colonoscopy</li> </ul>
<b>Treble and Thompson 2002</b> A 2.5-year-old girl ingested Pb pellets.	Time after ingestion <ul style="list-style-type: none"> <li>1.5 hours: 56</li> <li>29 hours: 35</li> <li>94 hours: 35</li> </ul>	No signs of toxicity observed	Laxatives
<b>Zardawi and Siriweera 2013</b> An 8-year-old boy ingested Pb pellets in game over a 2-year period.	Elevated PbB (17.4–27.4) over 2 years  Pellets observed in appendix	Hyperactivity	<ul style="list-style-type: none"> <li>Bowel irrigation</li> <li>Appendectomy</li> </ul>

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**Confounding Factors.** There are several uncertainties from case reports on ingestion of Pb debris. Therefore, it is not possible to determine dose, bioavailability, or accurate plasma-time concentration curves. Uncertainties include:

- Baseline PbB data are rarely available. Thus, it is difficult to determine the contribution of ingested Pb debris to measured PbB following ingestion.
- Time from ingestion of Pb debris to first clinical evaluation and PbB assessment is often unknown.
- No quantitative data on the dose of Pb ingested in debris are reported.
- No quantitative data on fecal excretion of ingested Pb are reported.
- Information on the chemical composition of Pb debris often is not reported.
- No information on potential differences in the bioavailability of different types of Pb debris is available

**Bioavailability of Pb Debris.** No quantitative estimates on the bioavailability of Pb debris in humans are available. Several case reports show increased PbB following ingestion of Pb debris, demonstrating that ingested Pb is absorbed (CDC 2006; Clifton et al. 2002; Durlach et al. 1986; Fergusson et al. 1997; Greensher et al. 1974; Guillard et al. 2006; Hatten et al. 2013; McKinney and McKinney 2000; McNutt et al. 2001; CDC 2004a; Mowad et al. 1998; Treble and Thompson 2002); see Table C-1 for details. However, due to lack of information on ingested dose, quantitative estimates of absorption cannot be determined. No information on bioavailability of Pb debris in animals was identified. Lead debris retained within the body will continue to contribute to elevated PbB until it is removed from the body, either spontaneously or by medical intervention (Banner et al. 2012; Clifton et al. 2002; Durlach et al. 1986; Gerhardsson et al. 2002; Guillard et al. 2006; McQuirter et al. 2004).

Lead debris must become bioaccessible (i.e., soluble) in the gastrointestinal tract in order for it to be absorbed. It is likely that processes thought to contribute to rendering ingested soil Pb bioaccessible also are important in rendering ingested Pb debris bioaccessible (see Section 3.1.1). IVBA assays that measure extractable Pb have not been evaluated for predicting bioavailability or RBA of ingested Pb debris, although one study found that IVBA measured at gastric pH predicted the relatively high *in vivo* RBA (100%) of firing range soils (Bannon et al. 2009; see Section 3.1.1).

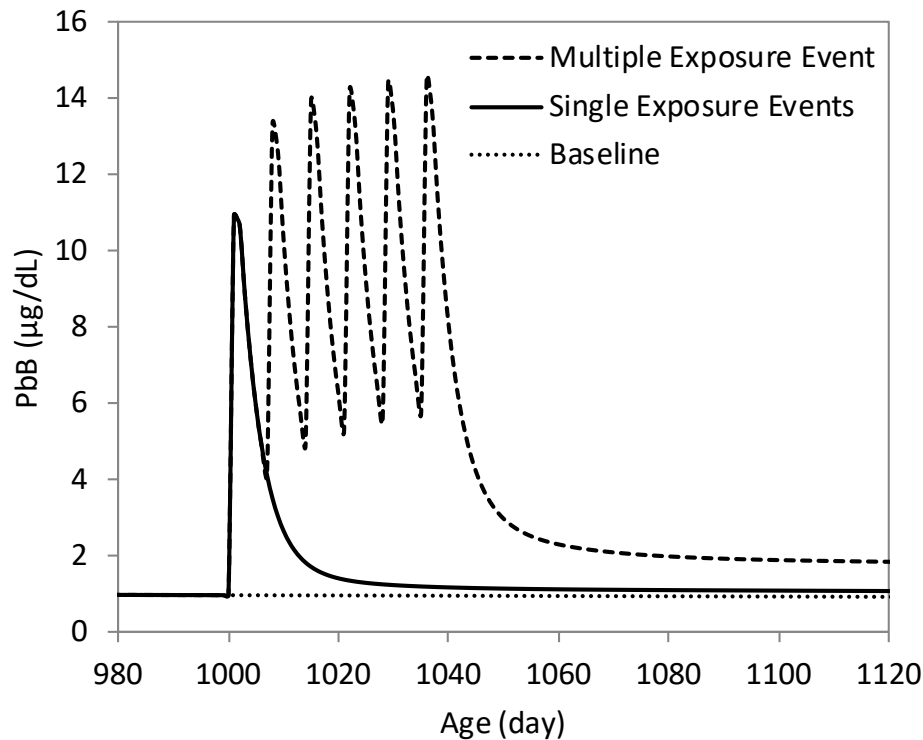
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Although dose-PbB relationships and bioavailability cannot be reliably established from the published case history of Pb debris ingestion, it is possible to use exposure-biokinetics models to reconstruct the time course of PbB expected for a given acute dose of soluble Pb and, from this, estimate the relative bioavailability of Pb from ingested Pb shot that would result in a given peak PbB. This scenario assumes that Pb debris is not retained in the body. The AALM-LG (EPA 2014a) can simulate the internal biokinetics of Pb associated with daily doses of Pb. This model predicts that a child 30 months of age who has a baseline PbB of 1 µg/dL would experience a 10 µg/dL increase in PbB in response to ingestion of approximately 1 mg of soluble Pb (Figure C-1). The peak PbB would occur during the day of ingestion and PbB would return to approximately 120% of baseline in approximately 35 days following the dose. If this prediction is extrapolated to the ingestion of Pb shot or other debris, the 1 mg dose of soluble Pb could occur in association with a dose of 100 mg of debris having an RBA of 1%, or 1 g of debris having an RBA of 0.1% (see Section 3.1.5.4 *EPA All Ages Lead Model [AALM]* for more information). Figure C-1 also shows the predicted PbB pattern for six repeated, weekly events in which the child ingested 1 mg of soluble PbB. This would result in periodic increases in PbB, with the maximum following each exposure event increasing until a pseudo-steady-state PbB was reached at approximately 14.5 µg/dL (13.5 µg/dL above baseline). The PbB would return to approximately 120% of baseline in approximately 570 days after the last exposure event. This longer time to baseline following multiple exposures reflects the accrual of Pb in bone with multiple dosing and the relatively slow transfer of Pb from bone to blood after exposure ceases (see Section 3.1).

Ingestion of soil from firing ranges may also contribute to PbB. A study in juvenile swine of eight soils (sieved to <250 µm) from small arms firing ranges showed a relative bioavailability range of 77–140%, with a mean of 108 % (SD or SE [not specified]: 18%). Soil from this site largely consisted of highly bioavailable Pb carbonate. However, this study did not provide information on bioavailability of Pb debris.

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**Figure C-1. PbB Predicted from AALM-LG for a 0.9 mg Dose of Soluble Pb Ingested by a Child 30 Months of Age**



***Retention of Pb Debris in the Appendix.*** Case reports show that Pb debris can be retained within the appendix (Banner et al. 2012; Cox and Pesola 2005; Durlach et al. 1986; Larsen and Blanton 2000; Lyons and Filston 1994; Madsen et al. 1988; Reddy 1985; Zardawi and Siriweera 2013); see Table C-1 for details. For this to occur, the appendix must be oriented with respect to the cecum in such a way to allow objects to pass through the appendiceal-cecal orifice; approximately 45% of the population have appendices with this orientation. However, approximately 65% of the population have appendices that might hinder foreign body access into the appendiceal lumen due to atypical anatomic position, adhesions, or kinks (Klingler et al. 1998). In addition to orientation of the appendix, the physical size and shape of the debris likely contribute to retention. Although it is not possible to determine the incidence of Pb debris lodged in the gastrointestinal tract or the appendix because not all cases of ingestion of Pb debris are reported in the published literature, approximately 45% of the population is predisposed to retention of Pb debris on orientation of the appendix.

***Toxicity of Ingested Pb Debris.*** Regardless of the source of Pb (e.g., ingested Pb debris, Pb paint, Pb-contaminated soil, occupational exposure), once Pb is absorbed into the body, toxicity will be related to PbB; thus, bioavailability and duration of elevated PbB, rather than the form of Pb ingested, will determine adverse health outcomes. If ingested Pb debris is not retained by the body, toxicity of PbB



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would be consistent with that described for acute Pb toxicity. A summary of peak PbBs and associated toxicity following exposure of ingested Pb debris is shown in Table C-2. Severity of toxicity increases with PbB. At PbB  $\leq 47$   $\mu\text{g/dL}$ , the only adverse health effect observed was a single report of headache at a PbB of 12  $\mu\text{g/dL}$ . With increased PbB, effects were observed in several organ systems and severity of effects increased. At a PbB range of 54–146  $\mu\text{g/dL}$ , abdominal colic, vomiting, hematological effects, and neurological effects were observed, and at a PbB of 180  $\mu\text{g/dL}$ , severe effects (seizure and cerebral edema) leading to death were observed. In most cases, the onset of toxicity occurs within hours or days of ingestion. If PbB remains elevated, either due to inadequate medical intervention or Pb that is retained within the body (i.e., appendix, gastrointestinal tract, etc.) adverse health effects associated with chronically elevated PbB would be expected to occur (see Chapter 2, Health Effects). As reviewed in Chapter 2, PbBs  $\leq 10$   $\mu\text{g/dL}$  are associated with adverse health effects to numerous organ systems, including developmental and neurological effects, with severity exhibiting dose-dependence. Given the many factors that can affect development of Pb-induced toxicity, case reports of individuals cannot provide generalizations of exposure-response relationships.

**Table C-2. Peak Blood Lead Concentration (PbB) and Acute Toxicity Associated with Ingestion of Lead (Pb) Debris**

Peak PbB ( $\mu\text{g/dL}$ ) <sup>a</sup>	Effects associated with Pb exposure	References
12–16	No effects observed	Fergusson et al. 1997
	Headache	Lyons and Filston 1994
40.5–47	No effects observed	Clifton et al. 2002; Hatten et al. 2013
54–61	No effects observed	Mowad et al. 1998; Treble and Thompson 2002
	Abdominal colic Hematological effects <sup>b</sup>	Banner et al. 2012
79	Abdominal colic and vomiting Hematological effects <sup>c</sup> Neurological effects <sup>d</sup>	McKinney and McKinney 2000
123	Abdominal colic, vomiting, diarrhea Hematological effects <sup>e</sup>	CDC 2004a
146	Vomiting Neurological signs <sup>f</sup>	Hatten et al. 2013
180	Vomiting Seizures Cerebral edema Death	CDC 2006

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**Table C-2. Peak Blood Lead Concentration (PbB) and Acute Toxicity Associated with Ingestion of Lead (Pb) Debris**

Peak PbB ( $\mu\text{g}/\text{dL}$ ) <sup>a</sup>	Effects associated with Pb exposure	References
391	Abdominal colic, gastrointestinal bleeding Anemia	McNutt et al. 2001

<sup>a</sup>Peak blood Pb reported.

<sup>b</sup>Elevated free erythrocyte protoporphyrin or microcytic anemia and increased blood zinc protoporphyrin.

<sup>c</sup>Decreased blood hemoglobin and hematocrit.

<sup>d</sup>“Mild” speech and language delays.

<sup>e</sup>Normocytic anemia, elevated protoporphyrin

<sup>f</sup>Decreased activity level and hyperactive patellar and brachioradialis reflexes.

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## APPENDIX D. QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances may find the following information helpful for fast answers to often-asked questions.

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### *Primary Chapters/Sections of Interest*

**Chapter 1: Relevance to Public Health:** The Relevance to Public Health Section provides an overview of exposure and health effects and evaluates, interprets, and assesses the significance of toxicity data to human health. A table listing minimal risk levels (MRLs) is also included in this chapter.

**Chapter 2: Health Effects:** Specific health effects identified in both human and animal studies are reported by type of health effect (e.g., death, hepatic, renal, immune, reproductive), route of exposure (e.g., inhalation, oral, dermal), and length of exposure (e.g., acute, intermediate, and chronic).

**NOTE:** Not all health effects reported in this section are necessarily observed in the clinical setting.

### **Pediatrics:**

**Section 3.2**      **Children and Other Populations that are Unusually Susceptible**  
**Section 3.3**      **Biomarkers of Exposure and Effect**

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### *ATSDR Information Center*

**Phone:** 1-800-CDC-INFO (800-232-4636) or 1-888-232-6348 (TTY)

**Internet:** <http://www.atsdr.cdc.gov>

The following additional materials are available online:

*Case Studies in Environmental Medicine* are self-instructional publications designed to increase primary health care providers' knowledge of a hazardous substance in the environment and to aid in the evaluation of potentially exposed patients (see <https://www.atsdr.cdc.gov/csem/csem.html>).

*Managing Hazardous Materials Incidents* is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident (see <https://www.atsdr.cdc.gov/MHMI/index.asp>). Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—*Medical Management Guidelines for Acute Chemical Exposures*—is a guide for health care professionals treating patients exposed to hazardous materials.

*Fact Sheets (ToxFAQs™)* provide answers to frequently asked questions about toxic substances (see <https://www.atsdr.cdc.gov/toxfaqs/Index.asp>).

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## APPENDIX D

***Other Agencies and Organizations***

*The National Center for Environmental Health (NCEH)* focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. Contact: NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 • Phone: 770-488-7000 • FAX: 770-488-7015 • Web Page: <https://www.cdc.gov/nceh/>.

*The National Institute for Occupational Safety and Health (NIOSH)* conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. Contact: NIOSH, 395 E Street, S.W., Suite 9200, Patriots Plaza Building, Washington, DC 20201 • Phone: 202-245-0625 or 1-800-CDC-INFO (800-232-4636) • Web Page: <https://www.cdc.gov/niosh/>.

*The National Institute of Environmental Health Sciences (NIEHS)* is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. Contact: NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 • Phone: 919-541-3212 • Web Page: <https://www.niehs.nih.gov/>.

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***Clinical Resources (Publicly Available Information)***

*The Association of Occupational and Environmental Clinics (AOEC)* has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. Contact: AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976 • FAX: 202-347-4950 • e-mail: [AOEC@AOEC.ORG](mailto:AOEC@AOEC.ORG) • Web Page: <http://www.aoec.org/>.

*The American College of Occupational and Environmental Medicine (ACOEM)* is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. Contact: ACOEM, 25 Northwest Point Boulevard, Suite 700, Elk Grove Village, IL 60007-1030 • Phone: 847-818-1800 • FAX: 847-818-9266 • Web Page: <http://www.acoem.org/>.

*The American College of Medical Toxicology (ACMT)* is a nonprofit association of physicians with recognized expertise in medical toxicology. Contact: ACMT, 10645 North Tatum Boulevard, Suite 200-111, Phoenix AZ 85028 • Phone: 844-226-8333 • FAX: 844-226-8333 • Web Page: <http://www.acmt.net>.

*The Pediatric Environmental Health Specialty Units (PEHSUs)* is an interconnected system of specialists who respond to questions from public health professionals, clinicians, policy makers, and the public about the impact of environmental factors on the health of children and reproductive-aged adults. Contact information for regional centers can be found at <http://pehsu.net/findhelp.html>.

*The American Association of Poison Control Centers (AAPCC)* provide support on the prevention and treatment of poison exposures. Contact: AAPCC, 515 King Street, Suite 510, Alexandria VA 22314 • Phone: 701-894-1858 • Poison Help Line: 1-800-222-1222 • Web Page: <http://www.aapcc.org/>.

## APPENDIX E. GLOSSARY

**Absorption**—The process by which a substance crosses biological membranes and enters systemic circulation. Absorption can also refer to the taking up of liquids by solids, or of gases by solids or liquids.

**Acute Exposure**—Exposure to a chemical for a duration of  $\leq 14$  days, as specified in the Toxicological Profiles.

**Adsorption**—The adhesion in an extremely thin layer of molecules (as of gases, solutes, or liquids) to the surfaces of solid bodies or liquids with which they are in contact.

**Adsorption Coefficient ( $K_{oc}$ )**—The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

**Adsorption Ratio ( $K_d$ )**—The amount of a chemical adsorbed by sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

**Benchmark Dose (BMD) or Benchmark Concentration (BMC)**—is the dose/concentration corresponding to a specific response level estimate using a statistical dose-response model applied to either experimental toxicology or epidemiology data. For example, a  $BMD_{10}$  would be the dose corresponding to a 10% benchmark response (BMR). The BMD is determined by modeling the dose-response curve in the region of the dose-response relationship where biologically observable data are feasible. The BMDL or BMCL is the 95% lower confidence limit on the BMD or BMC.

**Bioconcentration Factor (BCF)**—The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same period.

**Biomarkers**—Indicators signaling events in biologic systems or samples, typically classified as markers of exposure, effect, and susceptibility.

**Cancer Effect Level (CEL)**—The lowest dose of a chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and its appropriate control.

**Carcinogen**—A chemical capable of inducing cancer.

**Case-Control Study**—A type of epidemiological study that examines the relationship between a particular outcome (disease or condition) and a variety of potential causative agents (such as toxic chemicals). In a case-control study, a group of people with a specified and well-defined outcome is identified and compared to a similar group of people without the outcome.

**Case Report**—A report that describes a single individual with a particular disease or exposure. These reports may suggest some potential topics for scientific research, but are not actual research studies.

**Case Series**—Reports that describe the experience of a small number of individuals with the same disease or exposure. These reports may suggest potential topics for scientific research, but are not actual research studies.

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**Ceiling Value**—A concentration that must not be exceeded.

**Chronic Exposure**—Exposure to a chemical for  $\geq 365$  days, as specified in the Toxicological Profiles.

**Clastogen**—A substance that causes breaks in chromosomes resulting in addition, deletion, or rearrangement of parts of the chromosome.

**Cohort Study**—A type of epidemiological study of a specific group or groups of people who have had a common insult (e.g., exposure to an agent suspected of causing disease or a common disease) and are followed forward from exposure to outcome, and who are disease-free at start of follow-up. Often, at least one exposed group is compared to one unexposed group, while in other cohorts, exposure is a continuous variable and analyses are directed towards analyzing an exposure-response coefficient.

**Cross-sectional Study**—A type of epidemiological study of a group or groups of people that examines the relationship between exposure and outcome to a chemical or to chemicals at a specific point in time.

**Data Needs**—Substance-specific informational needs that, if met, would reduce the uncertainties of human health risk assessment.

**Developmental Toxicity**—The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

**Dose-Response Relationship**—The quantitative relationship between the amount of exposure to a toxicant and the incidence of the response or amount of the response.

**Embryotoxicity and Fetotoxicity**—Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the effect occurs. Effects include malformations and variations, altered growth, and *in utero* death.

**Epidemiology**—The investigation of factors that determine the frequency and distribution of disease or other health-related conditions within a defined human population during a specified period.

**Excretion**—The process by which metabolic waste products are removed from the body.

**Genotoxicity**—A specific adverse effect on the genome of living cells that, upon the duplication of affected cells, can be expressed as a mutagenic, clastogenic, or carcinogenic event because of specific alteration of the molecular structure of the genome.

**Half-life**—A measure of rate for the time required to eliminate one-half of a quantity of a chemical from the body or environmental media.

**Health Advisory**—An estimate of acceptable drinking water levels for a chemical substance derived by EPA and based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

**Immediately Dangerous to Life or Health (IDLH)**—A condition that poses a threat of life or health, or conditions that pose an immediate threat of severe exposure to contaminants that are likely to have adverse cumulative or delayed effects on health.

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**Immunotoxicity**—Adverse effect on the functioning of the immune system that may result from exposure to chemical substances.

**Incidence**—The ratio of new cases of individuals in a population who develop a specified condition to the total number of individuals in that population who could have developed that condition in a specified time period.

**Intermediate Exposure**—Exposure to a chemical for a duration of 15–364 days, as specified in the Toxicological Profiles.

**In Vitro**—Isolated from the living organism and artificially maintained, as in a test tube.

**In Vivo**—Occurring within the living organism.

**Lethal Concentration<sub>(LO)</sub> (LC<sub>LO</sub>)**—The lowest concentration of a chemical in air that has been reported to have caused death in humans or animals.

**Lethal Concentration<sub>(50)</sub> (LC<sub>50</sub>)**—A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

**Lethal Dose<sub>(LO)</sub> (LD<sub>LO</sub>)**—The lowest dose of a chemical introduced by a route other than inhalation that has been reported to have caused death in humans or animals.

**Lethal Dose<sub>(50)</sub> (LD<sub>50</sub>)**—The dose of a chemical that has been calculated to cause death in 50% of a defined experimental animal population.

**Lethal Time<sub>(50)</sub> (LT<sub>50</sub>)**—A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

**Lowest-Observed-Adverse-Effect Level (LOAEL)**—The lowest exposure level of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

**Lymphoreticular Effects**—Represent morphological effects involving lymphatic tissues such as the lymph nodes, spleen, and thymus.

**Malformations**—Permanent structural changes that may adversely affect survival, development, or function.

**Metabolism**—Process in which chemical substances are biotransformed in the body that could result in less toxic and/or readily excreted compounds or produce a biologically active intermediate.

**Minimal Risk Level (MRL)**—An estimate of daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse noncancer health effects over a specified route and duration of exposure.

**Modifying Factor (MF)**—A value (greater than zero) that is applied to the derivation of a Minimal Risk Level (MRL) to reflect additional concerns about the database that are not covered by the uncertainty factors. The default value for a MF is 1.



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**Morbidity**—The state of being diseased; the morbidity rate is the incidence or prevalence of a disease in a specific population.

**Mortality**—Death; the mortality rate is a measure of the number of deaths in a population during a specified interval of time.

**Mutagen**—A substance that causes mutations, which are changes in the DNA sequence of a cell's DNA. Mutations can lead to birth defects, miscarriages, or cancer.

**Necropsy**—The gross examination of the organs and tissues of a dead body to determine the cause of death or pathological conditions.

**Neurotoxicity**—The occurrence of adverse effects on the nervous system following exposure to a hazardous substance.

**No-Observed-Adverse-Effect Level (NOAEL)**—The dose of a chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Although effects may be produced at this dose, they are not considered to be adverse.

**Octanol-Water Partition Coefficient ( $K_{ow}$ )**—The equilibrium ratio of the concentrations of a chemical in *n*-octanol and water, in dilute solution.

**Odds Ratio (OR)**—A means of measuring the association between an exposure (such as toxic substances and a disease or condition) that represents the best estimate of relative risk (risk as a ratio of the incidence among subjects exposed to a particular risk factor divided by the incidence among subjects who were not exposed to the risk factor). An odds ratio that is greater than 1 is considered to indicate greater risk of disease in the exposed group compared to the unexposed group.

**Permissible Exposure Limit (PEL)**—An Occupational Safety and Health Administration (OSHA) regulatory limit on the amount or concentration of a substance not to be exceeded in workplace air averaged over any 8-hour work shift of a 40-hour workweek.

**Pesticide**—General classification of chemicals specifically developed and produced for use in the control of agricultural and public health pests (insects or other organisms harmful to cultivated plants or animals).

**Pharmacokinetics**—The dynamic behavior of a material in the body, used to predict the fate (disposition) of an exogenous substance in an organism. Utilizing computational techniques, it provides the means of studying the absorption, distribution, metabolism, and excretion of chemicals by the body.

**Pharmacokinetic Model**—A set of equations that can be used to describe the time course of a parent chemical or metabolite in an animal system. There are two types of pharmacokinetic models: data-based and physiologically-based. A data-based model divides the animal system into a series of compartments, which, in general, do not represent real, identifiable anatomic regions of the body, whereas the physiologically-based model compartments represent real anatomic regions of the body.

**Physiologically Based Pharmacodynamic (PBPD) Model**—A type of physiologically based dose-response model that quantitatively describes the relationship between target tissue dose and toxic endpoints. These models advance the importance of physiologically based models in that they clearly describe the biological effect (response) produced by the system following exposure to an exogenous substance.

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**Physiologically Based Pharmacokinetic (PBPK) Model**—A type of physiologically based dose-response model that is comprised of a series of compartments representing organs or tissue groups with realistic weights and blood flows. These models require a variety of physiological information, including tissue volumes, blood flow rates to tissues, cardiac output, alveolar ventilation rates, and possibly membrane permeabilities. The models also utilize biochemical information, such as blood:air partition coefficients, and metabolic parameters. PBPK models are also called biologically based tissue dosimetry models.

**Prevalence**—The number of cases of a disease or condition in a population at one point in time.

**Prospective Study**—A type of cohort study in which a group is followed over time and the pertinent observations are made on events occurring after the start of the study.

**Recommended Exposure Limit (REL)**—A National Institute for Occupational Safety and Health (NIOSH) time-weighted average (TWA) concentration for up to a 10-hour workday during a 40-hour workweek.

**Reference Concentration (RfC)**—An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer health effects during a lifetime. The inhalation RfC is expressed in units of mg/m<sup>3</sup> or ppm.

**Reference Dose (RfD)**—An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily oral exposure of the human population to a potential hazard that is likely to be without risk of deleterious noncancer health effects during a lifetime. The oral RfD is expressed in units of mg/kg/day.

**Reportable Quantity (RQ)**—The quantity of a hazardous substance that is considered reportable under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). RQs are (1) ≥1 pound or (2) for selected substances, an amount established by regulation either under CERCLA or under Section 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

**Reproductive Toxicity**—The occurrence of adverse effects on the reproductive system that may result from exposure to a hazardous substance. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

**Retrospective Study**—A type of cohort study based on a group of persons known to have been exposed at some time in the past. Data are collected from routinely recorded events, up to the time the study is undertaken. Retrospective studies are limited to causal factors that can be ascertained from existing records and/or examining survivors of the cohort.

**Risk**—The possibility or chance that some adverse effect will result from a given exposure to a hazardous substance.

**Risk Factor**—An aspect of personal behavior or lifestyle, an environmental exposure, existing health condition, or an inborn or inherited characteristic that is associated with an increased occurrence of disease or other health-related event or condition.

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**Risk Ratio/Relative Risk**—The ratio of the risk among persons with specific risk factors compared to the risk among persons without risk factors. A risk ratio that is greater than 1 indicates greater risk of disease in the exposed group compared to the unexposed group.

**Short-Term Exposure Limit (STEL)**—A STEL is a 15-minute TWA exposure that should not be exceeded at any time during a workday.

**Standardized Mortality Ratio (SMR)**—A ratio of the observed number of deaths and the expected number of deaths in a specific standard population.

**Target Organ Toxicity**—This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

**Teratogen**—A chemical that causes structural defects that affect the development of an organism.

**Threshold Limit Value (TLV)**—An American Conference of Governmental Industrial Hygienists (ACGIH) concentration of a substance to which it is believed that nearly all workers may be repeatedly exposed, day after day, for a working lifetime without adverse effect. The TLV may be expressed as a Time-Weighted Average (TLV-TWA), as a Short-Term Exposure Limit (TLV-STEL), or as a ceiling limit (TLV-C).

**Time-Weighted Average (TWA)**—An average exposure within a given time period.

**Toxicokinetic**—The absorption, distribution, metabolism, and elimination of toxic compounds in the living organism.

**Toxics Release Inventory (TRI)**—The TRI is an EPA program that tracks toxic chemical releases and pollution prevention activities reported by industrial and federal facilities.

**Uncertainty Factor (UF)**—A factor used in operationally deriving the Minimal Risk Level (MRL), Reference Dose (RfD), or Reference Concentration (RfC) from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using lowest-observed-adverse-effect level (LOAEL) data rather than no-observed-adverse-effect level (NOAEL) data. A default for each individual UF is 10; if complete certainty in data exists, a value of 1 can be used; however, a reduced UF of 3 may be used on a case-by-case basis (3 being the approximate logarithmic average of 10 and 1).

**Xenobiotic**—Any substance that is foreign to the biological system.

## APPENDIX F. ACRONYMS, ABBREVIATIONS, AND SYMBOLS

AAPCC	American Association of Poison Control Centers
ACGIH	American Conference of Governmental Industrial Hygienists
ACOEM	American College of Occupational and Environmental Medicine
ACMT	American College of Medical Toxicology
ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, and excretion
AEGL	Acute Exposure Guideline Level
AIC	Akaike's information criterion
AIHA	American Industrial Hygiene Association
ALT	alanine aminotransferase
AOEC	Association of Occupational and Environmental Clinics
AP	alkaline phosphatase
AST	aspartate aminotransferase
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
AWQC	Ambient Water Quality Criteria
BCF	bioconcentration factor
BMD/C	benchmark dose or benchmark concentration
BMD <sub>x</sub>	dose that produces a X% change in response rate of an adverse effect
BMDL <sub>x</sub>	95% lower confidence limit on the BMD <sub>x</sub>
BMDS	Benchmark Dose Software
BMR	benchmark response
BUN	blood urea nitrogen
C	centigrade
CAA	Clean Air Act
CAS	Chemical Abstract Services
CDC	Centers for Disease Control and Prevention
CEL	cancer effect level
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
Ci	curie
CI	confidence interval
cm	centimeter
CPSC	Consumer Products Safety Commission
CWA	Clean Water Act
DNA	deoxyribonucleic acid
DOD	Department of Defense
DOE	Department of Energy
DWEL	drinking water exposure level
EAFUS	Everything Added to Food in the United States
ECG/EKG	electrocardiogram
EEG	electroencephalogram
EPA	Environmental Protection Agency
ERPG	emergency response planning guidelines
F	Fahrenheit
F1	first-filial generation
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FR	Federal Register

## APPENDIX F

FSH	follicle stimulating hormone
g	gram
GC	gas chromatography
gd	gestational day
GGT	$\gamma$ -glutamyl transferase
GRAS	generally recognized as safe
HEC	human equivalent concentration
HED	human equivalent dose
HHS	Department of Health and Human Services
HPLC	high-performance liquid chromatography
HSDB	Hazardous Substance Data Bank
IARC	International Agency for Research on Cancer
IDLH	immediately dangerous to life and health
IRIS	Integrated Risk Information System
Kd	adsorption ratio
kg	kilogram
kkg	kilokilogram; 1 kilokilogram is equivalent to 1,000 kilograms and 1 metric ton
K <sub>oc</sub>	organic carbon partition coefficient
K <sub>ow</sub>	octanol-water partition coefficient
L	liter
LC	liquid chromatography
LC <sub>50</sub>	lethal concentration, 50% kill
LC <sub>Lo</sub>	lethal concentration, low
LD <sub>50</sub>	lethal dose, 50% kill
LD <sub>Lo</sub>	lethal dose, low
LDH	lactic dehydrogenase
LH	luteinizing hormone
LOAEL	lowest-observed-adverse-effect level
LSE	Level of Significant Exposure
LT <sub>50</sub>	lethal time, 50% kill
m	meter
mCi	millicurie
MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MF	modifying factor
mg	milligram
mL	milliliter
mm	millimeter
mmHg	millimeters of mercury
mmol	millimole
MRL	Minimal Risk Level
MS	mass spectrometry
MSHA	Mine Safety and Health Administration
Mt	metric ton
NAAQS	National Ambient Air Quality Standard
NAS	National Academy of Science
NCEH	National Center for Environmental Health
ND	not detected
ng	nanogram
NHANES	National Health and Nutrition Examination Survey
NIEHS	National Institute of Environmental Health Sciences

## APPENDIX F

NIOSH	National Institute for Occupational Safety and Health
NLM	National Library of Medicine
nm	nanometer
nmol	nanomole
NOAEL	no-observed-adverse-effect level
NPL	National Priorities List
NR	not reported
NRC	National Research Council
NS	not specified
NTP	National Toxicology Program
OR	odds ratio
OSHA	Occupational Safety and Health Administration
PAC	Protective Action Criteria
PAH	polycyclic aromatic hydrocarbon
PBPD	physiologically based pharmacodynamic
PBPK	physiologically based pharmacokinetic
PEHSU	Pediatric Environmental Health Specialty Unit
PEL	permissible exposure limit
PEL-C	permissible exposure limit-ceiling value
pg	picogram
PND	postnatal day
POD	point of departure
ppb	parts per billion
ppbv	parts per billion by volume
ppm	parts per million
ppt	parts per trillion
REL	recommended exposure level/limit
REL-C	recommended exposure level-ceiling value
RfC	reference concentration
RfD	reference dose
RNA	ribonucleic acid
SARA	Superfund Amendments and Reauthorization Act
SCE	sister chromatid exchange
SD	standard deviation
SE	standard error
SGOT	serum glutamic oxaloacetic transaminase (same as aspartate aminotransferase or AST)
SGPT	serum glutamic pyruvic transaminase (same as alanine aminotransferase or ALT)
SIC	standard industrial classification
SMR	standardized mortality ratio
sRBC	sheep red blood cell
STEL	short term exposure limit
TLV	threshold limit value
TLV-C	threshold limit value-ceiling value
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TWA	time-weighted average
UF	uncertainty factor
U.S.	United States
USDA	United States Department of Agriculture
USGS	United States Geological Survey
USNRC	U.S. Nuclear Regulatory Commission

## APPENDIX F

VOC	volatile organic compound
WBC	white blood cell
WHO	World Health Organization
>	greater than
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
γ	gamma
δ	delta
μm	micrometer
μg	microgram
q <sub>1</sub> *	cancer slope factor
-	negative
+	positive
(+)	weakly positive result
(-)	weakly negative result