0277
Lead and compounds (inorganic): CASRN 7439-92-1 (04/01/93)

Health risk assessment information on a chemical is included in IRIS only after a comprehensive review of chronic toxicity data by work groups composed of U.S. EPA scientists from several Program Offices. The summaries presented in Sections I and II represent a consensus reached in the review process. The other sections contain U.S. EPA information which is specific to a particular EPA program and has been subject to review procedures prescribed by that Program Office. The regulatory actions in Section IV may not be based on the most current risk assessment, or may be based on a current, but unreviewed, risk assessment, and may take into account factors other than health effects (e.g., treatment technology). When considering the use of regulatory action data for a particular situation, note the date of the regulatory action, the date of the most recent risk assessment relating to that action, and whether technological factors were considered. Background information and explanations of the methods used to derive the values given in IRIS are provided in the five Background Documents in Service Code 5, which correspond to Sections I through V of the chemical files.

STATUS OF DATA FOR Lead and compounds (inorganic)

File On-Line 03/01/88

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	message	02/01/91
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	on-line	05/01/91
Drinking Water Health Advisories (III.A.)	no data	
U.S. EPA Regulatory Actions (IV.)	on-line	06/01/92
Supplementary Data (V.)	no data	

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_I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

__I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Lead and compounds (inorganic)
CASRN -- 7439-92-1

A great deal of information on the health effects of lead has been obtained through decades of medical observation and scientific research. This information has been assessed in the development of air and water quality criteria by the Agency's Office of Health and Environmental Assessment (OHEA) in support of regulatory decision-making by the Office of Air Quality Planning and Standards (OAQPS) and by the Office of Drinking Water (ODW). By comparison to most other environmental toxicants, the degree of uncertainty about the health effects of lead is quite low. It appears that some of these effects, particularly changes in the levels of certain blood enzymes and in aspects of children's neurobehavioral development, may occur at blood lead levels so low as to be essentially without a threshold. The Agency's RfD Work Group discussed inorganic lead (and lead compounds) at two meetings (07/08/85 and 07/22/85) and considered it inappropriate to develop an RfD for inorganic lead. For additional information, interested parties are referred to the 1986 Air Quality Criteria for Lead (EPA-600/8-83/028a-dF) and its 1990 Supplement (EPA/600/8-89/049F) or the following Agency scientists:

Harlal Choudhury / ORD -- (513)569-7536 / FTS 684-7536

J. Michael Davis / ORD -- (919)541-4162 / FTS 629-4162

Jeff Cohen / ODW -- (202)260-5456 / FTS 260-5456

John Haines / OAQPS -- (919)541-5533 / FTS 629-5533

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Lead and compounds (inorganic)
CASRN -- 7439-92-1

Not available at this time.

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_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Lead and compounds (inorganic)
CASRN -- 7439-92-1
Last Revised -- 05/01/91

Section II provides information on three aspects of the carcinogenic risk assessment for the agent in question: the U.S. EPA classification, and quantitative estimates of risk from oral exposure and from inhalation exposure. The classification reflects a weight-of-evidence judgment of the likelihood that the agent is a human carcinogen. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. Background Document 2 (Service Code 5) provides details on the rationale and methods used to derive the carcinogenicity values found in IRIS. Users are referred to Section I for information on long-term toxic effects other than carcinogenicity.

__II.A. EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY

___II.A.1. WEIGHT-OF-EVIDENCE CLASSIFICATION

Classification -- B2; probable human carcinogen

Basis -- Sufficient animal evidence. Ten rat bioassays and one mouse assay have shown statistically significant increases in renal tumors with dietary and subcutaneous exposure to several soluble lead salts. Animal assays provide reproducible results in several laboratories, in multiple rat strains with some evidence of multiple tumor sites. Short term studies show that lead affects gene expression. Human evidence is inadequate.

___II.A.2. HUMAN CARCINOGENICITY DATA

Inadequate. There are four epidemiologic studies of occupational cohorts exposed to lead and lead compounds. Two studies (Dingwall-Fordyce and Lane, 1963; Nelson et al., 1982) did not find any association between exposure and cancer mortality. Selevan et al. (1985), in their retrospective cohort mortality study of primary lead smelter workers, found a slight decrease in the total cancer mortality (SMR=95). Apparent excesses were observed for

respiratory cancer (SMR=111, obs=41, p>0.05) and kidney cancer (SMR=204, obs=6, p>0.05). Cooper and Gaffey (1975) and Cooper (1985 update) performed a cohort mortality study of battery plant workers and lead smelter workers. They found statistically significant excesses for total cancer mortality (SMR=113, obs=344), stomach cancer (SMR=168, obs=34), and lung cancer (SMR=124, obs=109) in the battery plant workers. Although similar excesses were observed in the smelter workers, they were not statistically significant. Cooper and Gaffey (1975) felt it was possible that individual subjects were monitored primarily on the basis of obvious signs of lead exposure, while others who showed no symptoms of lead poisoning were not monitored.

All of the available studies lacked quantitative exposure information, as well as information on the possible contribution from smoking. All studies also included exposures to other metals such as arsenic, cadmium, and zinc for which no adjustment was done. The cancer excesses observed in the lung and stomach were relatively small (<200). There was no consistency of site among the various studies, and no study showed any dose-response relationship. Thus, the available human evidence is considered to be inadequate to refute or demonstrate any potential carcinogenicity for humans from lead exposure.

II.A.3. ANIMAL CARCINOGENICITY DATA

Sufficient. The carcinogenic potential of lead salts (primarily phosphates and acetates) administered via the oral route or by injection has been demonstrated in rats and mice by more than 10 investigators. The most characteristic cancer response is bilateral renal carcinoma. Rats given lead acetate or subacetate orally have developed gliomas, and lead subacetate also produced lung adenomas in mice after i.p. adminstration. Most of these investigations found a carcinogenic response only at the highest dose. The lead compounds tested in animals are almost all soluble salts. Metallic lead, lead oxide and lead tetralkyls have not been tested adequately. Studies of inhalation exposure have not been located in the literature.

Azar et al. (1973) administerd 10, 50, 100, and 500 ppm lead as lead acetate in dietary concentrations to 50 rats/sex/group for 2 years. Control rats (100/sex) received the basal laboratory diet. In a second 2-year feeding study, 20 rats/group were given diets containing 0, 1000, and 2000 ppm lead as lead acetate. No renal tumors were reported in the control groups or in treated animals of either sex receiving 10 to 100 ppm. Male rats fed 500, 1000, and 2000 ppm lead acetate had an increased renal tumor incidence of 5/50, 10/20, and 16/20, while 7/20 females in the 2000-ppm group developed renal tumors.

The Azar et al. (1973) study is limited by the lack of experimental detail. The possibility of environmental contamination from lead in the air

or drinking water was not mentioned. The strains of rats used were not specified in the study, but the Health Effects Assessment for Lead (U.S. EPA, 1984) indicates the rats were Wistar strain. The weight gain at 1000 and 2000 ppm was reported to be depressed, but details were not given.

Kasprzak et al. (1985), in investigating the interaction of dietary calcium on lead carcinogenicity, fed 1% lead subacetate (8500 ppm Pb) to male Sprague-Dawley rats in the diet for 79 weeks. Of the rats surviving (29/30) in this treatment group beyond 58 weeks, 44.8% had renal tumors. Four rats had adenocarcinomas; the remainaing nine had adenomas. Bilateral tumors were noted. No renal tumors were noted among the controls.

As part of a study to determine interactions between sodium nitrite, ethyl urea and lead, male Sprague-Dawley rats were given lead acetate in their drinking water for 76 weeks (Koller et al., 1986). The concentration of lead was 2600 ppm. No kidney tumors were detected among the 10 control rats. Thirteen of 16 (81%) lead-treated rats had renal tubular carcinoma; three tumors were detected at 72 weeks and the remainder detected at the termination of the study.

Van Esch and Kroes (1969) fed basic lead acetate at 0, 0.1%, and 1.0% in the diet to 25 Swiss mice/sex/group for 2 years. No renal tumors developed in the control group, but 6/25 male mice of 0.1% basic lead acetate group had renal tumors (adenomas and carcinomas combined). In the 1.0% group, one female had a renal tumor. The authors thought that the low incidence in the 1.0% group was due to early mortality.

Hamsters given lead subacetate at 0.5% and 1% in the diet had no significant renal tumor response (Van Esch and Kroes, 1969).

II.A.4. SUPPORTING DATA FOR CARCINOGENICITY

Lead acetate induces cell transformation in Syrian hamster embryo cells (DiPaolo et al., 1978) and also enhances the incidence of simian adenovirus induction. Lead oxide showed similar enhanced adenovirus induction (Casto et al., 1979).

Under certain conditions lead compounds are capable of inducing chromosomal aberrations in vivo and in tissue cultures. Grandjean et al. (1983) showed a relationship between SCE and lead exposure in exposed workers. Lead has been shown, in a number of DNA structure and function assays, to affect the molecular processes associated with the regulation of gene expression (U.S. EPA, 1986).

__II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSURE

Not available.

Quantifying lead's cancer risk involves many uncertainties, some of which may be unique to lead. Age, health, nutritional state, body burden, and exposure duration influence the absorption, release, and excretion of lead. In addition, current knowledge of lead pharmacokinetics indicates that an estimate derived by standard procedures would not truly describe the potential risk. Thus, the Carcinogen Assessment Group recommends that a numerical estimate not be used.

__II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION EXPOSURE

Not available.

__II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS (CARCINOGENICITY ASSESSMENT)

___II.D.1. EPA DOCUMENTATION

U.S. EPA. 1984. Health Effects Assessment for Lead. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Emergency and Remedial Response, Washington, DC. EPA/540/1-86/055. NTIS PB85-163996/AS.

U.S. EPA. 1986. Air Quality Criteria Document for Lead. Volumes III, IV. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC, for the Office of Air Quality Planning and Standards. EPA-600/8-83/028dF.

U.S. EPA. 1987. Preliminary review of the carcinogenic potential of lead associated with oral exposure. Prepared by the Office of Health and Environmental Assessment, Carcinogenic Assessment Group, Washington DC, for the Office of Drinking Water, Office of Solid Waste and the Office of Emergency and Remedial Response (Superfund). OHEA-C-267. Internal Review

Draft.

___II.D.2. REVIEW (CARCINOGENICITY ASSESSMENT)

The review of the carcinogenic potential of lead associated with oral exposure has received Agency review.

The 1986 Air Quality Criteria Document for Lead has received Agency and External Review.

Agency Work Group Review: 05/04/88

Verification Date: 05/04/88

___II.D.3. U.S. EPA CONTACTS (CARCINOGENICITY ASSESSMENT)

William Pepelko / ORD -- (202)260-5898 / FTS 260-5898

James Cogliano / ORD -- (202)260-9243 / FTS 260-9243

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_III. HEALTH HAZARD ASSESSMENTS FOR VARIED EXPOSURE DURATIONS

__III.A. DRINKING WATER HEALTH ADVISORIES

Substance Name -- Lead and compounds (inorganic)
CASRN -- 7439-92-1

Not available at this time.

__III.B. OTHER ASSESSMENTS

Substance Name -- Lead and compounds (inorganic)

CASRN -- 7439-92-1

Content to be determined.

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_IV. U.S. EPA REGULATORY ACTIONS

Substance Name -- Lead and compounds (inorganic)
CASRN -- 7439-92-1
Last Revised -- 06/01/92

EPA risk assessments may be updated as new data are published and as assessment methodologies evolve. Regulatory actions are frequently not updated at the same time. Compare the dates for the regulatory actions in this section with the verification dates for the risk assessments in sections I and II, as this may explain inconsistencies. Also note that some regulatory actions consider factors not related to health risk, such as technical or economic feasibility. Such considerations are indicated for each action. In addition, not all of the regulatory actions listed in this section involve enforceable federal standards. Please direct any questions you may have concerning these regulatory actions to the U.S. EPA contact listed for that particular action. Users are strongly urged to read the background information on each regulatory action in Background Document 4 in Service Code 5.

__IV.A. CLEAN AIR ACT (CAA)

___IV.A.1. NATIONAL AMBIENT AIR QUALITY STANDARD (NAAQS)

Considers technological or economic feasibility? -- No

Discussion -- Under Section 109 of the CAA, EPA has set a primary (health-based) NAAQS for lead of 1.5 ug/cu.m, calendar quarter average not to be exceeded (43 FR 41258, 10/05/78). The secondary (welfare-based) NAAQS is identical to the primary standard. EPA is currently reviewing these standards to determine if changes are warranted.

Reference -- 40 CFR 50.12

U.S. EPA Contact -- Air Quality Management Division / OAQPS /
(919)541-5656 / FTS 629-5656

IV.B. SAFE DRINKING WATER ACT (SDWA)

IV.B.1. MAXIMUM CONTAMINANT LEVEL GOAL (MCLG) for Drinking Water

Value (status) -- 0 mg/L (Final, 1991)

Considers technological or economic feasibility? -- NO

Discussion -- The MCLG for lead is zero based on (1) occurrence of low level effects and difficulties in identifying clear threshold levels, (2) the overall Agency goal of reducing total lead exposures, and (3) the classification of lead as a group B2 carcinogen.

Reference -- 56 FR 26460 (06/07/91); 56 FR 32112 (07/15/91)

EPA Contact -- Health and Ecological Criteria Division / OST / (202) 260-7571 / FTS 260-7571; or Safe Drinking Water Hotline / (800) 426-4791

IV.B.2. MAXIMUM CONTAMINANT LEVEL (MCL) for Drinking Water

Value -- None (Final, 1991)

Considers technological or economic feasibility? -- YES

Discussion -- EPA concluded that setting an MCL for lead is not feasible and believes that the treatment approach contained in the final rule (corrosion control, source water reduction, public education and lead service line problems associated with establishing MCL's.

Monitoring requirements -- Tap water monitoring for lead and copper to determine whether a system is subject to the treatment technique requirements. Water quality parameter sampling to determine the effectiveness of optional corrosion control treatment. Source water monitoring for lead and copper to determine source water's contribution to total tap water lead and copper levels, and the need for treatment. Monitoring schedules vary by system size and type of monitoring.

Analytical methodology -- Atomic absorption/furnace technique (EPA 239.2; ASTM D-3559-85D; SM 3113); inductively-coupled plasma/mass spectrometry (EPA 200.8); atomic absorption/platform furnace technique (EPA 200.9).

Best available technology --

Optimal corrosion control treatment: pH/akalinity adjustment, calcium adjustment: addition of corrosion inhibitor.

Source water treatment: Coagulation/filtration: ion exchange: lime softening: reverse osmosis.

Public education.

Lead service line replacement.

Reference -- 45 FR 57332 (08/27/80): 53 FR 31517 (08/18/88): 56 FR 26460 (06/07/91): 56 FR 32112 (07/15/91).

EPA Contact -- Drinking Water Standards Division / OGWDW / (202) 260-7575 / FTS 260-7575: or Safe Drinking Water Hotline / (800) 426-4791

___IV.B.3. SECONDARY MAXIMUM CONTAMINANT LEVEL (SMCL) for Drinking Water

No data available

___IV.B.4. REQUIRED MONITORING OF "UNREGULATED" CONTAMINANTS

No data available

__IV.C. CLEAN WATER ACT (CWA)

___IV.C.1. AMBIENT WATER QUALITY CRITERIA, Human Health

Water and Fish Consumption -- 5.0E+1 ug/L

Fish Consumption Only -- None

Considers technological or economic feasibility? -- NO

Discussion -- The criterion was set at the existing drinking water standard in 1980.

Reference -- 45 FR 79318 (11/28/80)

EPA Contact -- Criteria and Standards Division / OWRS
(202)260-1315 / FTS 260-1315

___IV.C.2. AMBIENT WATER QUALITY CRITERIA, Aquatic Organisms

Freshwater:

Acute -- 8.2E+1 ug/L (1-hour average)
Chronic -- 3.2E+0 ug/L (4-day average)

Marine:

Acute -- 1.40E+2 ug/L (1-hour average)
Chronic -- 5.6E+0 ug/L (4-day average)

Considers technological or economic feasibility? -- NO

Discussion -- Criteria were derived from a minimum data base consisting of acute and chronic tests on a variety of species. The toxicity of this compound in freshwater is hardness dependent. The values given are for a hardness of 100 mg/L CaCO3. For a more complete discussion, see the referenced notice.

Reference -- 50 FR 30784 (07/29/85)

EPA Contact -- Criteria and Standards Division / OWRS
(202)260-1315 / FTS 260-1315

__IV.D. FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT (FIFRA)

No data available

__IV.E. TOXIC SUBSTANCES CONTROL ACT (TSCA)

No data available

__IV.F. RESOURCE CONSERVATION AND RECOVERY ACT (RCRA)

___IV.F.1. RCRA APPENDIX IX, for Ground Water Monitoring

Status -- Listed (total lead)

Reference -- 52 FR 25942 (07/09/87)

EPA Contact -- RCRA/Superfund Hotline
(800)424-9346 / (202)260-3000 / FTS 260-3000

__IV.G. SUPERFUND (CERCLA)

___IV.G.1. REPORTABLE QUANTITY (RQ) for Release into the Environment

Value (status) -- 1 pound (Statutory, 1987)

Considers technological or economic feasibility? -- NO

Discussion -- The statutory 1-pound RQ for lead is retained pending assessment of its potential carcinogenicity and may be adjusted in a future notice of proposed rulemaking when the evaluation of available data is completed. Lead was evaluated for chronic toxicity, but was not ranked for toxicity because of insufficient data.

Reference -- 52 FR 8140 (03/16/87); 54 FR 33418 (08/14/89)

EPA Contact -- RCRA/Superfund Hotline
(800)424-9346 / (202)260-3000 / FTS 260-3000

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_V. SUPPLEMENTARY DATA

Substance Name -- Lead and compounds (inorganic)
CASRN -- 7439-92-1

Not available at this time.

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_VI. BIBLIOGRAPHY

Substance Name -- Lead and compounds (inorganic)
CASRN -- 7439-92-1
Last Revised -- 12/01/89

__VI.A. ORAL RfD REFERENCES

None

__VI.B. INHALATION RfD REFERENCES

None

__VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

Anderson, E.L., and CAG (Carcinogenic Assessment Group). 1983. Quantitative approaches in use to assess cancer risk. Risk Analysis. 3: 277-295.

Azar, A., H.J. Trochimowicz and M.E. Maxfield. 1973. Review of lead studies in animals carried out at Haskell Laboratory - Two year feeding study and response to hemorrhage study. In: Barth D., A. Berlin, R. Engel, P. Recht and J. Smeets, Ed. Environmental health aspects of lead: Proceedings International Symposium: October 1972: Amsterdam, The Netherlands. Commission of the European Communities, Luxemberg. p. 199-208.

Casto, B.C., J. Meyers and J.A. DiPaolo. 1979. Enhancement of viral transformation for evaluation of the carcinogenic or mutagenic potential of

inorganic metal salts. Cancer Res. 39: 193-198.

Cooper, W.C. 1985. Mortality among employees of lead battery plants and lead producing plants, 1947-1980. Scand. J. Work Environ. Health. 11: 331-345.

Cooper, W.C. and W.R. Gaffey. 1975. Mortality of lead workers. In: Proceedings of the 1974 Conference on Standards of Occupational Lead Exposure, J.F. Cole, Ed., February, 1974. Washington, DC. J. Occup. Med. 17: 100-107.

Dingwall-Fordyce, I. and R.E. Lane. 1963. A follow-up study of lead workers. Br. J. Ind. Med. 20: 313-315.

DiPaolo, J.A., R.L. Nelson and B.C. Casto. 1978. In vitro neoplastic transformation of Syrian hamster cells by lead acetate and its relevance to environmental carcinogenesis. Br. J. Cancer. 38: 452-455.

Grandjean, P., H.C. Wulf and E. Niebuhr. 1983. Sister chromatid exchange in response to variations in occupational lead exposure. Environ. Res. 32: 199-204.

Kasprzak, K.S., K.L. Hoover and L.A. Poirier. 1985. Effects of dietary calcium acetate on lead subacetate carcinogenicity in kidneys of male Sprague-Dawley rats. Carcinogenesis. 6(2): 279-282.

Koller, L.D., N.I. Kerkvliet and J.H. Exon. 1986. Neoplasia induced in male rats fed lead acetate, ethyl urea and sodium nitrate. Toxicol. Pathol. 13: 50-57.

Nelson, D.J., L. Kiremidjian-Schumacher and G. Stotzky. 1982. Effects of cadmium, lead, and zinc on macrophage-mediated cytotoxicity toward tumor cells. Environ. Res. 28: 154-163.

Selevan, S.G., P.J. Landrigan, F.B. Stern and J.H. Jones. 1985. Mortality of lead smelter workers. Am. J. Epidemiol. 122: 673-683.

Van Esch, G.J. and R. Kroes. 1969. The induction of renal tumors by feeding of basic lead acetate to mice and hamsters. Br. J. Cancer. 23: 265-271.

U.S. EPA. 1984. Health Effects Assessment for Lead. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Emergency and Remedial Response, Washington, DC. EPA/540/1-86/055. NTIS PB85-163996/AS.

U.S. EPA. 1986. Air Quality Criteria Document for Lead. Volumes III, IV. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC, for the Office of Air Quality Planning and Standards. EPA-600/8-83/028dF.

U.S. EPA. 1987. Preliminary review of the carcinogenic potential of lead associated with oral exposure. Prepared by the Office of Health and Environmental Assessment, Carcinogenic Assessment Group, Washington DC, for the Office of Drinking Water, Office of Solid Waste and the Office of Emergency and Remedial Response (Superfund). OHEA-C-267. Internal Review Draft.

VI.D. DRINKING WATER HA REFERENCES

None

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VII. REVISION HISTORY

Substance Name -- Lead and compounds (inorganic)
CASRN -- 7439-92-1

Date	Section	Description
09/26/88	II.	Carcinogen summary on-line
02/01/89	IV.B.1.	Effect level corrected in discussion
06/01/89	II.D.3.	Primary contact changed
06/01/89	IV.A.1.	Reference corrected - changed number for part in CFR
12/01/89	II.A.3.	Last paragraph - Correct Van Esch 1969 citation
12/01/89	VI.	Bibliography on-line
07/01/90	I.A.	Changed contact J. Cohen's office and telephone number
07/01/90	IV.F.1.	EPA contact changed
02/01/91	I.A.	Message revised to include new EPA document
02/01/91	I.A.	EPA contacts changed
05/01/91	II.A.	Text edited
01/01/92	IV.	Regulatory actions updated
06/01/92	IV.B.2.	MCL monitoring reqs. and BAT corrected

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SYNONYMS

Substance Name -- Lead and compounds (inorganic)
CASRN -- 7439-92-1
Last Revised -- 03/01/88

7439-92-1
Lead
Lead and compounds
plumbum