

WORKING DRAFT
SUPPORT FOR THE CHEMICAL NOMINATION AND SELECTION
PROCESS OF THE NATIONAL TOXICOLOGY PROGRAM

NIEHS CONTRACT No. N01-ES-5-5097

EXECUTIVE SUMMARY OF DATA

LEAD OXIDE/LEAD SULFIDE

August 20, 1987
Rev. April 25, 1988*
May 22, 1989

Submitted to:

National Toxicology Program
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I. Chemical and Physical Information

The chemical and physical properties of, lead oxide (PbO) and lead sulfide (PbS) are presented in Table 1.

II. Production/Use/Exposure/Environmental/Regulatory Data

A. Production

1. Manufacturing Process

The four commercially important processes for manufacturing PbO all involve the air oxidation of molten metallic lead, rapid cooling of the product, and, in three of the processes, milling the resultant coarse particles. In all cases, the product must be cooled quickly to $<300^{\circ}\text{C}$ to avoid the formation of red lead (Pb_3O_4) (Sittig, 1978).

PbS is produced by heating metallic lead in sulfur vapor (Kirk-Othmer, 1984), or by passing hydrogen sulfide gas into an acid solution of lead nitrate (Hawley, 1981). PbS is found in nature as the mineral galena (Hawley, 1981).

*The National Institute for Occupational Safety and Health has nominated lead oxide and lead sulfide (galena) for comparative toxicological study by the inhalation route.

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Table 1. Chemical and Physical Properties of Lead Oxide and Lead Sulfide		
-	Lead Oxide	Lead Sulfide
-	-	-
A. <u>Synonyms:</u>	Lead monoxide	Lead monosulfide
	Lead (2+) oxide	Lead (2+) sulfide
	Plumbous oxide	Plumbous sulfide
	Litharge	Galena
B. <u>CAS No.:</u>	1317-36-8	1314-87-0
C. <u>Molecular Formula:</u>	PbO	PbS
D. <u>Molecular Weight:</u>	223.21	239.28
E. <u>Physical Properties</u>	-	-
1. <u>Physical State:</u>	Exists in two forms:	
	red to reddish-yellow, tetragonal crystals stable at ordinary temperatures; yellow, orthorhombic crystals stable above 489°C (Windholz, 1983)	Silvery, metallic crystals or black powder (Hawley, 1981); black powder (Windholz, 1983)
2. <u>Melting Point:</u>	888°C (yellow crystalline form) (Hawley, 1981)	1,114°C (Hawley, 1981)
3. <u>Boiling Point:</u>	-- ^a	--
4. <u>Flash Point:</u>	--	--
5. <u>Vapor Pressure:</u>	--	--
6. <u>Specific Gravity:</u>	9.53 (yellow form) (Hawley, 1981)	7.13-7.7 (Hawley, 1981)
7. <u>Refractive Index:</u>	--	--
8. <u>Solubility in Water:</u>	Insoluble (Windholz, 1983)	Insoluble (Windholz, 1983); 0.01244 g/100 mL at 20° C (Kirk-Othmer, 1984)
9. <u>Solubility in Organic Solvents:</u>	Soluble in acetic acid; insoluble in alcohol (Windholz, 1983)	--
10. <u>Log Partition Coefficient(s):</u>	--	--
11. <u>Other:</u>	Soluble in dilute nitric acid (Windholz, 1983) and alkalies (Hawley, 1981)	Soluble in nitric and dilute hydrochloric acids (Windholz, 1983); insoluble in alkalies (Hawley, 1981)

^aNo information was found.

2. Volume

PbO

The public portion of the Toxic Substances Control Act (TSCA) Chemical Substances Inventory (TSCA Inventory)

reported U.S. production of between 302.3 and 1,423 million lbs. of PbO in 1977 (refer to Enclosure 1; USEPA 1987). This volume was the output of 13 manufacturers; 5 other manufacturers did not report production volume data for 1977.

The U.S. International Trade Commission (USITC) reports production volume data only for organic chemicals and therefore did not report domestic production volume for PbO for the years 1981-1985 (USITC, 1982a, 1983a, 1984a, 1985, 1986).

The Chemical Economics Handbook (CEH) did not report domestic production volume data for PbO (CEH, 1986).

The public portion of the TSCA Inventory reported the importation of from 2.1 to 21 million pounds of PbO in 1977 (refer to Enclosure 1; USEPA, 1987). This volume was imported by five companies; one other company reported zero importation and two others did not report import volume data for 1977.

The U.S. Department of Commerce (USDOC) reported the following volumes of PbO imported for the years 1983 through 1985 (USDOC, 1984-1986):

<u>Year</u>	<u>Import Volume (lb)</u>
1983	25,410,092
1984	28,055,225
1985	21,945.689

Neither the CEH, nor the USITC reported import volume for PbO (CEH, 1986; USITC, 1982b, 1983b, 1984b).

PbS

The public portion of the TSCA Inventory reported U.S. production of between 1 and 10 million pounds of PbS in 1977 (refer to Enclosure 2; USEPA, 1987). This volume was the output of two manufacturers; one other manufacturer reported zero production and another did not report production volume data for 1977.

Neither the CEH nor the USITC reported domestic production volume data for PbS (CEH, 1986; USITC 1982a-1984a, 1985, 1986).

No information was found on the importation of PbS in the TSCA Inventory (USEPA, 1987), the USDOC (1984-1986), the USITC (1982b-1984b) or in the CEH (1986).

3. Producers and Importers

Producers

The following companies were listed as manufacturers of PbO in the public portion of the TSCA Inventory (refer to Enclosure 1; USEPA 1987):

ASARCO, Inc.
Denver, CO
El Paso, TX
East Helena, MT

Atlantic Steel Company
Atlanta, GA

Cerac, Inc.
Milwaukee, WI

Chloride Metals
Columbus, GA
Florence, MS
Tampa, FL

Daelco, Inc.

City of Commerce, CA

Douglas Battery Mfg. Co.
Winston-Salem, NC

Engelhard Industries Div.
Newark, NJ

ESB, Inc.
Allentown, PA
Atlanta, GA
Dallas, TX
Fairfield, CT
Kansas City, MO
Logansport, IN
Los Angeles, CA
Memphis, TN
Richmond, KY
Sumter, SC

General Battery Corp.
City of Industry, CA
Dallas, TX
Frankfort, IN
Greer, SC
Muhlenberg Twp, PA
Salina, KS

Globe-Union, Inc.
Atlanta, GA
Bennington, VT
Geneva, IL
Louisville, KY
Middletown, DE
Milwaukee, WI
Owasso, MI
St. Joseph, MO

Gould Inc., Metals Div.
Dunmore, PA
Frisco, TX
St. Paul, MN

Hammond Lead Products, Inc.
Hammond, IN
Stowe, PA

Haven Chemical
Philadelphia, PA

NL Industries, Inc.
Atlanta, Ga
Brooklyn, NY
Charleston, WV
Chicago, IL
Dallas, TX
Los Angeles, CA
Philadelphia, PA
Portland, OR
St. Louis, MO

Powerlab Inc.
Terrell, TX

Reichhold Chemicals, Inc.
Brooklyn, NY

RSR-Quemetco
City of Industry, CA
Seattle, WA

Standard Electric Co. Inc.
San Antonio, TX

Additional producers reported by SRI International (1986) are:

Associated Lead Incorporated
Philadelphia, PA

Eagle-Picher Industries, Inc.
Joplin, MO

The public portion of the TSCA Inventory listed the following manufacturers of PbS (refer to Enclosure 2; USEPA, 1987):

Cerac, Inc.
Milwaukee, WI

Eagle-Picher Industries, Inc.
Galena, IL

Orion Research, Inc.
Cambridge, MA

SCM Corporation
Hammond, IN

SRI International (1986) listed the manufacture of PbS by one of the above companies at a different location:

Eagle-Picher Industries Inc.
Joplin, MO

Importers

The following companies were listed as importers of PbO in the public portion of the TSCA Inventory (refer to Enclosure 1; USEPA, 1987):

American Cyanamid Company
Chicago, IL

BASF Wyandotte Corp.
Parsippany, NJ

Corning Glass Works
Corning, NY

Indussa-Div. of African Metals
New York, NY

Pemco Products
Baltimore, MD

Philipp Bros. Chemicals, Inc.
New York, NY

Robert H. Webber Company, Inc.
Stamford, CT

United Mineral & Chemical Corp.
New York, NY

No information was found on importers of PbS.

4. Technical Product Composition

PbO is available in the following grades: Chemically Pure (containing no detectable impurities), fused, and powdered (Hawley, 1981).

PbS is available in technical, Chemically Pure, electronic (Hawley, 1981), and high purity (99.999%) grades (Kirk-Othmer 1984).

B. Use

PbO is used in storage batteries, glazing pottery, glass flux for painting porcelain and glass, lead glass, and with glycerol in metal cement. It is also used in ointments and plasters and in preparing lead subacetate solutions. Other uses include producing iridescent colors on brass and bronze; for coloring sulfur-containing substances such as hair, nails, wool, and horn; as a pigment for rubber; for use in oil refining, varnishes, paints, and enamels; and in assays for precious metal ores (Hawley, 1981; Windholz, 1983).

PbS is used in photoconductive cells, infrared detectors, transistors, humidity sensors in rockets, and as a catalyst for removing mercaptans from petroleum distillates. It is also used in mirror coatings, high-temperature solid-film lubricants, and in blue lead pigments (Kirk-Othmer, 1984) as well as in glazing earthenware (Windholz, 1983).

C. Occupational Exposure

(i) PbO

The National Occupational Hazard Survey (NOHS), conducted by the National Institute for Occupational Safety and Health (NIOSH) from 1972 to 1974, estimated that 678,394 workers in 63,005 plants were potentially exposed to PbO in the workplace (NIOSH, 1976). The estimates were derived from the use of tradename products known to contain PbO (4%) and the use of generic products suspected of containing the compound (96%). The largest numbers of exposed workers were in the special-trade contractors, transportation equipment, electrical equipment & supplies, wholesale trade, machinery (except electrical), printing and publishing, and primary metal industries (refer to Enclosure 3). The occupational groups with the largest numbers of exposed workers were plumbers and pipe fitters, assemblers, electricians, sheet-metal workers and tinmiths, auto mechanic, construction laborers (except carpenter helpers), heavy equipment mechanics including diesel), and miscellaneous machine operatives (refer to Enclosure 4).

Preliminary data from a second workplace survey, the National Occupational Exposure Survey (NOES), conducted by NIOSH from 1980 to 1983, indicated that 513 workers, including 47 women, at 101 sites were potentially exposed to PbO in the workplace in 1980 (NIOSH, 1984). The industry with the largest number of exposed workers was transportation equipment and the occupational group with the largest number of exposed workers was miscellaneous machine operators (not elsewhere classified) (refer to Enclosure 5). Unlike NOHS, the NOES estimates were based on direct observation by the surveyor of the actual use of compound.

(ii) PbS

The NOHS conducted by NIOSH from 1972 to 1974 estimated that 5,462 workers in 589 plants were potentially exposed to PbS in the workplace (NIOSH, 1976). These estimates were derived solely from the use of generic products suspected of containing PbS (100%). The largest numbers of exposed workers were in the food and kindred products, electrical equipment and supplies, and special-trade contractors (refer to enclosure 6). The occupational groups with the largest numbers of exposed workers were miscellaneous machine operatives, not specified laborers, and bulldozer operators (refer to Enclosure 7).

Preliminary data from a second workplace survey, the NOES, conducted by NIOSH from 1980 to 1983, indicated that seven workers (number of women not specified) in seven plants were potentially exposed to PbS in the workplace in 1980 (NIOSH, 1984). All of these exposed workers were employed as engineering technicians (not elsewhere classified) in the business service industry (refer to Enclosure 8). Unlike NOHS, the NOES estimates were based only on direct observation by the surveyor of the actual use of the compound.

Neither the NOHS nor the NOES databases contain information on the frequency, level, or duration of exposure of workers to any of the chemicals listed therein. They are surveys that only provide

estimates of workers potentially exposed to the chemicals.

The Mine Safety and Health Administration (MSHA) estimates that about 1,600 workers, mostly miners, are currently exposed to lead sulfide (Haartz, 1987).

The NIOSH Tradename Ingredient Data Base of NOHS listed PbO as a constituent of 44 products used in industrial applications (NIOSH, 1976). The concentration of PbO in the products ranged from 1 to 99%, with 7 products containing 1-10%, 16 products containing 11-50%, 8 products containing 51-70%, and 13 products containing 71-99% PbO.

The American Conference of Government Industrial Hygienists (ACGIH) has not adopted a threshold limit value for either PbO or PbS. However, the ACGIH has adopted an 8-hour time-weighted average (TWA) threshold limit value of 0.15 mg/m^3 Pb for exposure to inorganic lead dusts and fumes (ACGIH, 1986).

NIOSH has recommended a 10-hour TWA of $<0.1 \text{ mg/m}^3$ Pb for inorganic lead fumes and dusts (NIOSH, 1985a).

D. Consumer Exposure

PbO is listed in the U.S. Consumer Product Safety Commission's (USCPSC's) Chemicals in Products database as being used in paints and coatings and adhesives. PbS is not listed in this database. This database, however, was compiled over 10 years ago and has not been updated. The presence of PbO or PbS in current consumer products has not been verified (USCPSC, 1987).

E. Environmental Data

No information was found on the releases, ambient environmental concentrations, or environmental fate of either PbO or PbS.

F. Regulatory Status

USEPA's Effluent Guidelines for the Lead Monoxide Production Subcategory of the Inorganic Chemicals Manufacturing Point Source Category are zero discharge for new and existing point sources and 2.0 mg/L (1-day maximum) and 1.0 mg/L (maximum 30-day average) for discharge to publicly owned treatment works (USEPA, 1986b).

A reportable quantity of 5,000 pounds (2,270 kg) for release from vessels and facilities has been established for PbS under the Comprehensive Environmental Response, Compensation, and Liability Act (USEPA, 1986a).

The MSHA exposure standard is 150 mg lead/m^3 for miners, who are exposed mostly to lead sulfide, and 50 mg lead/m^3 for workers in the general industry, who are exposed mostly to lead oxide (Haartz, 1987).

No other Federal regulations relating specifically to PbO or PbS were found.

Johnson and Mason (1984) have reviewed the regulatory history and regulatory status of lead and its compounds, including a summary of U.S. agencies regulating lead. In many cases, the Federal agencies do not distinguish between elemental lead and lead salts. Six federal agencies have lead regulations:

Environmental Protection Agency
Consumer Product Safety Commission
Small Business Administration
Housing and Urban Development
Food and Drug Administration
Department of Labor

Neither PbO nor PbS have been scored or studied by the TSCA Interagency Testing Committee (ITS, 1985).

III. Toxicological Effects

A. Human Data

1. Acute: No information was found on PbO or PbS.

Gosselin et al. (1984) rated most lead compounds to be moderately to very toxic with a probable oral lethal dose of 0.05 to 5 g/kg.

Acute lead poisoning in adults causes anemia, colic, headache, fatigue, "gumline", and peripheral neuropathy. In children the symptoms include vomiting, anorexia, lethargy, convulsions, coma, and encephalopathy (Damstra, 1977). Children surviving acute lead encephalopathy suffer permanent damage to the central nervous system (Venugopal and Luckey, 1978).

2. Epidemiological Evidence/Case Reports: Feldman et al. (1977) reported the effects of PbO fumes in demolition workers (burners) exposed to high levels of lead for a period of 1 month. The average atmospheric concentration for 32 burners was 4.36 mg/m^3 , while the mean was 0.23 mg/m^3 for 12 nonburners. The burners experienced nausea, abdominal discomfort, mood change and irritability, sleeplessness, fatigue, headache, and numbness and tingling of the extremities. In addition, the mean peroneal motor-nerve conduction velocity was significantly ($p < 0.02$) lower in 13 burners when compared to 6 nonburners.

From 1977 to 1980 in Kuwait, Shaltout et al. (1981) observed lead encephalopathy in infants aged between 1 and 18 months. The source of lead was an eye cosmetic surma or kohl, containing 45 to 88% PbS. In 11 infants, kohl (containing over 75% lead) was applied to the conjunctival surfaces of the eyelids, eyebrows, and umbilicus of the newborns and was also used by their lactating mothers. Two of the infants died from acute lead encephalopathy. Clinical Findings in the infants with lead encephalopathy included vomiting, convulsions, irritability, pallor, bulging fontanelle, status epilepticus, stupor, and paralysis of upward gaze. Laboratory findings showed a mean blood lead level of 5.42 mmol/L , anemia, basophilic stippling of the red blood cells, reticulocytosis, elevated levels of cerebrospinal fluid protein, and coproporphyrinuria.

Healy et al. (1984) reported lead-induced convulsions in an infant born to a mother who was a regular user of grey kohl containing 80% (w/w) PbS. At 90 days of age, the infant was pale with increased fontanelle tension. Radiology of the long bones and skull showed lead lines and sutured diastasis. Laboratory tests showed anemia, reticulocytosis, pronounced basophilic stippling, elevated levels of cerebrospinal fluid protein, and a blood lead level of 6.3 mmol/L .

3. Chemical Disposition: Blood lead levels of 30 to $> 120 \text{ mg/100 mL}$ were measured in men occupationally exposed to PbO (O'Riordan and Evans 1974; Garza-Chapa et al., 1977).

Aslam et al. (1980) observed high blood lead levels in Asian children following application of the eye cosmetic surma containing varying amounts of lead. About 20 mg of surma is deposited in the conjunctivae at each application. The mean blood lead level of 62 surma users was $1.65 \pm 0.68 \text{ mmol/L}$, while the mean was $0.98 \pm 0.42 \text{ mmol/L}$ in nonusers ($p < 0.001$). Regular applications for over 2 years of surma containing 86% lead to a child caused the child's blood lead level to rise from 2.4 to 3.4 mmol/L .

Blood lead levels of 50 mg/100 mL were measured in two men exposed to 50 mg/m^3 of lead dust consisting of a mixture of lead oxides and lead sulfate (93% of particles 0.5 - 5 μm) for one hour (Schutz and Skerfving, 1976). Increases in

blood lead levels of about 45 mg/100 ml were observed in two men exposed to 250 mg/m³ lead concentrate dust (primarily lead sulfide) for one hour (Nygren and Carlsson, 1983). Nygren and Carlsson (1983) compared these two studies and concluded that the blood lead level was proportional to the soluble portion of the inhaled lead.

In a study of 15 mill workers exposed to lead sulfide, a significant relationship of blood lead and urinary d-aminolevulinic acid (ALA to respirable lead, but not to total lead, was found among non-smokers. Among smokers, there was no relationship of blood lead with either respirable or total lead (Roy, 1977). In an earlier study two groups of 16 galena (PbS) mill workers were exposed to air concentrations of lead of up to 8 mg/m³. Average blood lead concentrations of 18 and 26 mg/100 ml were found in these groups (Belden and Garber, 1949).

In a NIOSH study lead miners and mill workers were found to be exposed to up to 77 mg/m³ of respirable lead. Blood lead levels were lower in miners than in mill workers, and were higher in welders than in nonwelders. It was speculated that the welding effect was due to production of lead oxide (Petsonk and Hewett, 1983).

4. **Biochemical Effects:** No information was found relevant to the toxicity of PbO or PbS.
5. **Carcinogenicity/Chronic:** No information was found on the carcinogenicity or chronic toxicity of PbO or PbS.
6. **Teratogenicity and Reproductive Effects:** No information was found on PbO or PbS.

B. Animal Data

1. **Acute:** Venugopal and Lucky (1978) reported an intraperitoneal LD₅₀ of 400 mg/kg for PbO in rats and 1600 mg/kg for PbS in rats and guinea pigs. No information was given on the strain, sex, or number of animals used.

Fairhall and Sayers (1940) studied the toxicity of 11 organic compounds to guinea pigs by ingestion, inhalation, and intraperitoneal injection. Lead sulfide was observed to be less toxic than lead oxide by all routes. Details on the protocol were either limited or not provided.

2. **Chemical Disposition:** Griffin et al. (1975) studied the effects of continuous exposure to airborne PbO particulates in Sprague-Dawley rats and rhesus monkeys. Thirty-six rats and four monkeys of each sex were exposed to PbO particulates at an average concentration of 21.5 mg lead/m³, 22 hours/day, 7 days/week for 6 months or 1 year. An equal number of rats and two monkeys of each sex served as unexposed controls. The mean concentration of lead in the diet was 0.50 mg/g for the rat and 0.46 mg/g for the monkey; the drinking water contained <3 mg/L lead. In both species, blood lead levels reached a maximum during the first few months of exposure and did not increase significantly thereafter; the concentration in exposed rats was 28 mg/100 mL and in exposed monkeys was 16 mg/100 mL compared to 3.7 mg/100 mL in the control animals. After cessation of exposure (time not specified), blood lead levels decreased to about 5 mg/100 mL in both species.

Elevated levels of lead were observed in bone, liver, kidney, and lungs of both species. While lead levels were generally below 1 mg Pb/g tissue in control animals, they rose to between 2 and 4 mg Pb/g tissue in soft tissues of exposed animals. The largest concentrations were found in bone where they rose to slightly more than 5 mg Pb/g tissue in exposed rats and 7 mg Pb/g tissue in exposed monkeys. There were no major differences between lead

levels in animals exposed for 6 or 12 months. Lead concentrations averaged higher both in the urine and feces of exposed rats and monkeys than in control animals. In rats maintained for 6 month after termination of exposure (recovery period), lead levels decreased in the soft tissue, but remained elevated in the bone; no data were given for monkeys.

No information was found on PbS.

3. Biochemical Effects: No information was found relevant to the toxicity of PbO or PbS.

4. Prechronic: No information was found on PbO or PbS.

5. Carcinogenicity/Chronic: Kobayashi and Okamoto (1974) reported that intratracheal instillation of PbO in combination with benzo(a)pyrene [B(a)P] induced lung tumors in Syrian golden hamsters. Groups of 15 male and 15 female hamsters received 1 mg PbO (purity 99.8%); 1 mg B(a)P; mg PbO + 1 mg B(a)P; or 0.2 mL of 0.5 carboxymethyl-cellulose-isotonic saline solution (vehicle control) once a week for 10 weeks; an equal number of animals served as untreated controls. Ninety-five percent of the PbO and B(a)P particles were <10 μ m. The hamsters were sacrificed 60 weeks after the first instillation. Those that received PbO, B(a)P, or PbO B(a)P showed lower survival rates than the untreated controls. No lung tumors were observed in hamsters treated with PbO, B(a)P, or the vehicle solution alone. No respiratory tract lesions were observed in the vehicle and untreated control animals. PbO alone induced bronchiolar alveolar metaplasias in a total of 19 animals and adenomatous proliferation of the lung in three animals. PbO and B(a)P in combination induced adenomas in 9 animals, an adenocarcinoma in the peripheral area of the lung, bronchioalveolar metaplasias in 23 animals, adenomatous proliferations in 5 animals, and atypical epithelial proliferation in one animal. No pathological changes were observed in the trachea or the large bronchi.

Griffin et al. (1975) observed no gross, microscopic, or ultrastructural changes in the tissues or changes in serum chemistry or hematology parameters of Sprague-Dawley rats or rhesus monkeys exposed to PbO particulates at an average concentration of 21.5 mg Pb/m for up to 1 year. (See section III. B.2. for experimental details). A marked, but reversible, reduction in erythrocyte a-aminolevulinic acid dehydrase was observed after 12 months of exposure.

Zook et al. (1980) administered PbO via an oropharyngeal tube 3 to 5 times/week for 44 to 277 days to 13 subadult squirrel monkeys; two monkeys served as controls. The dosage, adjusted periodically, averaged 1.95 to 4.57 mg/kg/week. Gross and microscopic examinations of the brains were conducted. Four treated monkeys died (study days 133, 232, 258, and 277); one was sacrificed moribund on study day 63 and the remaining 8 were sacrificed between study days 44 and 227. "Most" of the animals lost weight, and convulsions were observed in six of the treated monkeys brain lesions were observed in nine treated monkeys; signs did not correlate well with lesions. Severe cerebral lesions, convulsions, and death occurred in three monkeys; two others fed the same or higher mean doses (not specified) showed no histologic lesions but did experience convulsions. Encephalopathy varied from negative to marked.

No information was found on the carcinogenicity or chronic toxicity of PbS.

6. Teratogenicity and Reproductive Effects: No information was found on PbO or PbS.

C. Genotoxicity

PbO was nonmutagenic in the rec assay with Bacillus subtilis strains H17 (rec⁺) and M45 (rec⁻) (Kanematsu et al., 1980).

Schwanitz et al. (1970) and Garza-Chapa et al. (1977) observed chromatid and chrcosomal aberrations in cultured lymphocytes of men occupationally exposed to PbO. On the other hand, O'Riordan and Evans (1974) did not observe chromosomal damage in the peripheral blood lymphocytes of men chronically exposed to PbO.

No information was found on PbS.

D. Structure-Activity Relationships

Chronic exposure to inorganic lead produces adverse effects on the hematopoietic, renal, and nervous systems. Lead causes anemia resulting from a reduction in the life-span of red blood cells and impairment of heme synthesis. The effect on the kidneys consists of a nonspecific nephropathy. At high levels of exposure, lead causes encephalopathy and many survivors of encephalopathy sustain residual brain damage. Lead also induces colic and may exert toxic action on the heart (WHO, 1980).

International Agency for Research on Cancer (IARC, 1982) concluded that there was sufficient evidence for the carcinogenicity of some lead salts in experimental animals.

Lead acetate, lead subacetate, and lead phosphate were carcinogenic to rats, and lead subacetate was carcinogenic to mice, inducing renal tumors following their oral or parenteral administration. Gliomas occurred in rats given oral administration of lead acetate or lead subacetate. Intraperitoneal injection of lead subacetate increased the incidence of lung adenomas in mice. Lead dimethyldithiocarbamate was not carcinogenic to mice or rats following its oral administration. Other lead salts and lead tetraalkyls have not been tested adequately (IARC, 1982). IARC (1982) also concluded that there was inadequate evidence for the carcinogenicity of lead or lead compounds in humans.

PbO and PbS have not been previously been selected for testing by the National Toxicology Program (NTP) (NTP CHEMTRACK, 1988).

The NTP testing status of compounds structurally related to PbO and PbS is summarized in Table 2 (NTP CHEMTRACK, 1988)

IV. Nomination Source*

- A. Source: National Institute for Occupational Safety and Health (NIOSH, 1985b)
- B. Recommendation: Comparative toxicological study of lead oxide lead sulfide (galena) by inhalation route.

Table 2. NTP Testing Status of Compounds Structurally Related to PbO and PbS				
Chemical	CAS No.	Genotoxicity	Carcinogenicity	Other
Lead acetate	15347-57-6	--	--	Neurobehavior study completed
Lead (2+) acetate	301-04-2	Negative in <i>Salmonella</i> Negative in mouse lymphoma assay in two independent studies	Chronic feeding study completed, positive control	Two continuous breeding studies completed
Lead dimethyl-dithiocarbamate	19010-66-3	Positive in <i>Salmonella</i> On test in mouse lymphoma assay Negative for sex-linked recessive lethal mutations in <i>Drosophila</i> Positive for chromosomal aberrations and sister chromatid exchanges in CHO cells	Feeding study, negative in rats and mice	--
Lead dioxide	1309-60-0	Negative in <i>Salmonella</i>	--	--

C. **Rationale/Remarks:** Ascertain whether lead oxide and lead sulfide have comparable toxicities

D. **Priority:** None given

E. **Date of Nomination:** December 1985

* Following deferral of these chemicals by the Chemical Evaluation Committee on September 29, 1987 (see below), NTP staff contacted NIOSH for further information on the types of studies recommended by the agency. NIOSH provided the following additional information:

F. **Recommendations:**

- Acute and subchronic inhalation of lead oxide and lead sulfide
- Determine relationship between respirable exposure concentration and blood levels in acute studies
- Examine the following endpoints in subchronic studies:
 1. Lead levels in whole blood and serum
RBC fragility, free erythrocyte protoporphyrin, blood ALA dehydrogenase

2. Renal parameters such as urinary concentrating ability
heme precursors: ALA, porphobilinogen,
coproporphyrin
3. Gross and histopathology

- Other endpoints to be considered:

1. Immunological - humoral and cell mediated assays
2. Neurophysiological - startle reflex response
3. Reproductive - Male: testicular and epididymal weights, semen profile
- Female: estrus cycle rates

G. Rationale/Remarks:

About 1,600 workers, mostly miners, who are exposed to lead sulfide, are subject to MSHA's 150 mg/m³ standard. The available toxicity data on lead oxide and lead sulfide do not allow NIOSH and MSHA to conclude that these workers are adequately protected. NIOSH and MSHA need data on the relationship between exposure concentrations and blood lead as well as the toxicity of lead sulfide and lead oxide at comparable lead concentrations. They will use these data in their review of the current standard for miners.

VI. Board of Scientific Counselors Review

- A. Date of Review: May 17, 1988
- B. Recommendations: -Acute comparative toxicity studies of lead and lead sulfide
- C. Priority: High
- D. Rationale/Remarks:
 - Concern over lead toxicity
 - Studies should include determination of blood lead levels, and investigation of biomarkers
 - NTP should propose a study to investigate the neurotoxicity of lead and its salts, in particular, their effect on brain development; proposed study to be submitted to Board for review

VII. Executive Committee Review:

- A. Date of Review: August 18, 1988
- B. Decision: Selected as NTP Fiscal Year 1988 priority chemicals for in-depth toxicological evaluation.

VIII. Information Sources

This report was prepared by a multidisciplinary team of scientists and technicians. Mr. Jess Rowland was the principal author.

The information resources used in preparing this review include the automated databases listed below, journal articles, general reference materials, and contractor/agency reports.

ON-LINE DATABASES SEARCHED

<u>MEDLARS</u>		
CHEMLINE	-	-
RTECS	-	-
HSDB	-	-
MEDLINE	-	1983-Present
TOXLINE	-	1966-Present
TOX 76	-	1976-1980
TOX 65	-	1940-1975
CANCERLIT	-	1963-Present
CANCERPROJ	-	1978-1981
-	-	-
<u>DIALOG</u>		
BIOSYS PREVIEWS	-	1969-Present
CHEMICAL EXPOSURE	-	1974-Present
CIN (Chemical Indust. Notes)	-	1974-Present
CONFERENCE PAPAERS INDEX	-	1973-Present
CRGS (Chemical Regulations and Guidelines System)	-	1982-Present
EMBASE	-	1974-Present
ENVIROLINE	-	1971-Present
ENVIRONMENTAL BIBLIOGRAPHY	-	1974-Present
FEDERAL REGISTER ABSTRACTS	-	1977-Present
FEDERAL RESEARCH IN PROGRESS	-	1976-Present
FSTA (Food Science and Technology Abstracts)	-	1969-Present
IPA (International Pharmaceutical Abstracts)	-	1970-Present
LIFE SCIENCES COLLECTION	-	1978-Present
NTIS	-	1970-Present
OCCUPATIONAL SAFETY AND HEALTH	-	1972-Present
PTS PROMT	-	1972-Present
POLLUTION ABSTRACTS	-	1970-Present
SCISEARCH	-	1974-Present
WORLD TEXTILES	-	1970-Present
-	-	-
<u>CIS</u>		
OHMTADS	-	-
SPHERE, CESARS, DERMAL, ENVIROFATE, GENETOX, and ISHOW	-	-
-	-	-
<u>BRS</u>		
KIRK-OTHMER	-	1978-Present
-	-	-
<u>INFOLINE</u>		

LABORATORY HAZARD BULLETIN	-	1981-Present
CURRENT AWARENESS IN BIOLOGICAL SCIENCES	-	1983-Present
CHEMICAL HAZARDS IN INDUSTRY	-	1984-Present
WORLD SURFACE COATING ABSTRACTS	-	1976-Present
-	-	-
<u>OTHERS</u>		
ITS	-	-
NOES	-	-
NOHS	-	-
NTP CHEMTRACK	-	-
STORET	-	-
TSCA INVENTORY	-	-
HAZARDLINE	-	1983-Present
CAS ONLINE	-	-

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