TO: C-1531

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Original could not be located. Correction made to page 1 on 5-8-89 changing CAS no. from 50825-29-1 to 61790-14-5 and CAS name from cyclohexanecarboxylic acid, lead salt to naphthenic acids lead salts. Original had a note attached indicating approval of B.W. Karch, M.D.

N 27667

ES-3606

HASKELL LABORATORY

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This review reflects the available toxicity literature, both published and unpublished. Studies have not been evaluated for scientific merit. Contact Haskell Laboratory if you have questions.

Common Name: Lead Naphthenate
Chemical Name: Naphthenic acids, lead salts (61790-14-5)
Cyclohexanecarboxylic acid, lead salt (50825-29-1)
Synonyms: Nuodex (Tenneco Chem. Inc.)
Ferro Naphthenate (Ferro Corp.)
CAS Registry No.: 61790-14-5

Chemical Structure: Lead naphthenate is a complex mixture of lead salts of organic acids obtained during the manufacturing of hydrocarbon distillates; principal components include cyclopentanoic and cyclohexanoic acid salts.

Physical Properties (11):

Description:	Transparent, yellow liquid (24% Pb)
Molecular Weight:	1578.52
Boiling Point:	> 150°C @ 760 mm Hg
Melting Point:	----
Density/Specific Gravity:	1.15 (25/25°C)
Vapor Pressure:	< 5 mm Hg @ 25°C
Flash Point/Flammability:	100°F (Tag closed cup)
Explosive Limits:	1.1-6%
Solubility:	Nearly insoluble in water
Conversion Factors:	----

This literature search contains 8 pages of text and 26 references.

This search was prepared by Richard C. Graham. See the last page of this document for its updating history.

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Exposure Standards:

Du Pont AEL = 50 ug/m^3 (as lead) (8-hour TWA).
OSHA PEL = 50 ug/m^3 (as lead) (8-hour TWA) (5).

DOT Classification:

None.

EPA RCRA Status:

None.

FDA Status:

None.

TSCA Inventory:

Yes.

TOXICITY

Summary*

Lead naphthenate (24% Pb) has very low acute oral toxicity with an LD50 in rats of 5100 mg/kg. While no deaths occurred in rabbits administered up to 8 mL/kg of the 24% solution, contact with the skin of animals and man shows lead naphthenate can be absorbed through the skin. Workers exposed to an average lead naphthenate concentration of 96 ug/m^3 had a mean blood-lead level of 63 ug/dL. Lead naphthenate was not mutagenic in the Ames test. Renal tumors were observed in mice dermally administered a 20% solution in benzene for up to 569 days.

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* See Related Reference 26 for a review on lead naphthenate.

A. Acute

1. Oral

- LD50 (rats) = 4404 mg/kg* (3.83 mL/kg) (14).
- LD50 (rats) = 5100 mg/kg* (20).

2. Skin

- Groups of five rabbits were administered 1, 2, 4, or 8 mL/kg of a 24% lead naphthenate solution. No deaths occurred, and no irritation was noted. The only adverse effect was a retardation in regrowth of hair at the site of application (14).
- No skin irritation occurred in mice treated twice weekly with a 20% solution of lead naphthenate in benzene (1).
- A skin loading experiment was performed on three men whose skin was exposed to 6 mL of an oil containing 192 mg of lead as lead naphthenate. After 5, 10, 30, 60, 210, and 480 minutes, the lead content of the venous blood was determined. The lead content had increased within ten minutes after application, and reached more than 300% of its initial value after 30 to 60 minutes. The lead concentration returned to its initial value within 480 minutes (16).

3. Eyes

- No information is available.

4. Inhalation

- In an aluminum forging plant where lead naphthenate was sprayed without local ventilation, the mean concentration of lead naphthenate in the air was 96 ug/m^3 with a range of 12-430 ug/m^3. The 29 workers exposed to the lead naphthenate had a mean blood-lead concentration of 63 ug/dL which was significantly higher than that of 103 unexposed controls (blood lead concentration of 17 ug/dL) (12).

5. Injection Studies

a. Intraperitoneal

- LD50 (rats) = 520 mg/kg* (20).

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* 24% lead naphthenate solution

B. Extended Studies

1. Oral

- A group of 20 rats was administered 0.25 mL of a 1% (as lead) lead naphthenate solution daily for four weeks. No abnormal characteristics in appearance or behavior were noted. Histopathological examination did not reveal any abnormal changes (20).

- Rats were fed a diet containing 100 ppm of lead naphthenate or 1% of a dried film coated with lead naphthenate. The duration of the study was 12 weeks. About 50% of the administered lead was found in the gut. A maximum lead concentration was reached in the kidney and liver in two weeks and this concentration remained steady for 12 weeks. In bone, a constant level was reached after eight weeks (10).

- See Related References 23-25 for additional information.

2. Skin

a. Animal Studies

- Rats were administered 500 uL of a 0.24 M lead naphthenate solution to the skin at the back of their necks. The rats were dosed on alternate days and were sacrificed two days after the fifth dose. No effect was noted on the growth of these rats. Lead was found in all organs with the highest level found in the kidneys followed by the liver and spleen. delta-Aminolevulinic dehydratase (ALA-D) activity of the liver tissues was inhibited (18).

- Groups of ten rabbits were treated six hours a day for ten days with 1 mL of a paint containing 1.2 or 6% lead naphthenate. Rabbits were held for 29 days after the last treatment for blood lead evaluations. Blood samples were taken before treatment and on days five, ten, 15, and 39. A dose-response was noted, but the absorption in the 6% group was only 1.5-fold greater than that of the 1.2% group. In the group treated with 1.2% lead naphthenate, blood lead values reached a peak by day five and leveled off by day ten. The level did not change much during the next five days (day 15). However, by day 29, lead values had dropped from a mean of 263.9 ug/L at day 15 to 142.0 ug/L at day 29. At day 39, the level had dropped still further to 82 ug/L. A similar pattern was noted in the 6% group (8).

- Four test oils containing from 0.55 to 1.35% lead as lead naphthenate were applied (1 mL/kg/day) to the clipped backs of 20 rabbits. The treatments were eight hours a day, five days a week, for four weeks. Cardiac blood samples were obtained before the first application and 24 hours after the fifth, tenth, fifteenth, and twentieth application. Mean pretreatment baseline lead levels ranged from 0.23 to 0.34 ppm. Posttreatment values ranged from 0.74 to 1.0 ppm (13).

- A cutting oil containing 0.8 grams of lead per 100 mL was absorbed through the skin of guinea pigs. It caused an increase of the basophilic granulation of the red blood cells and an increase in the lead content of the liver. These results were similar when the oil was applied to the back or the neck of the guinea pigs. Application on the neck, however, caused deaths within one month (6).

- A cutting oil containing a sulfur compound in addition to lead was non-toxic to guinea pigs in experiments in which the skin was treated for 65 days to concentrations encountered by workers (7).

- Rats were administered 80-200 mg/kg of lead as lead naphthenate for eight weeks and also administered 0, 5, 10, or 15 ppm of selenium in their drinking water. The growth rate and food consumption of rats receiving both lead and selenium approached a normal rate while rats treated only with lead showed hampered growth rate and lower food consumption. ALA-D in whole blood, liver, and kidney were depressed in the lead only rats but normal in rats receiving both lead and selenium (19).

- Groups of five rabbits were administered 1, 2, or 4 mL/kg/day of a 24% lead naphthenate solution for up to 90 days. Growth retardation was noted in the 2 and 4 mL/kg groups. Anemia developed in the rabbits administered 1 and 2 mL/kg. Anemia did not develop in the high-dose rabbits. Because these rabbits died after a significantly shorter exposure period, it is possible that the time of exposure was not sufficient for anemia to develop. Mortality occurred in all three groups (4/5, 4/5, and 5/5, respectively). The LT50s were 55, 40, and 22.5 days, respectively. The primary cause of death was a severe pneumonia (14).

- A group of 59 mice were treated twice a week with a 20% lead naphthenate solution in benzene. The duration of the study was 569 days. No malignant skin tumors were found. Seven mice (11%) had benign skin papillomas, the first after 193 days of treatment. Four mice (7%) developed renal adenomas, and one (2%) developed a renal carcinoma. No control group was included in this study (1,2).

b. Human Studies

- Gear oil containing 1.35% lead naphthenate was applied to the skin of ten men over 20 days. A total of 0.81 grams of lead in 60 mL of oil was applied. Mean pretreatment baseline blood-lead values were 0.37 ppm. Blood lead values were 0.71 ppm at five days; 0.66 ppm at ten days; 0.69 ppm at 15 days; and 0.61 ppm at 20 days. No indications of altered physiology, biochemical changes or lead intoxication were noted (13).

- A study of 14 people exposed to lead naphthenate for periods ranging from four months to 12 years showed variable blood and urinary lead levels. Examination of blood samples from two volunteers at intervals up to 240 minutes after dermal application of mineral oil containing lead naphthenate showed that transcutaneous absorption of lead can take place (17).

2. Subcutaneous Injection

- A group of six rats was administered 500 uL of 0.24 M lead naphthenate on alternate days until five doses had been given. The rats were less responsive to a needle prick after the second dose. Weakness and incoordination of the legs were noted after the second dose. One rat died 28 hours after the third dose, and another died 30 hours after the fourth dose. Paralysis of the front and hind legs was observed in both of these rats a few hours prior to death. ALA-D activity of liver tissues was inhibited. Body weights decreased by 10% during the experimental period. An increase in lead content was observed in all examined organs. As excreting organs, the kidneys possessed the highest level of lead followed by the liver and spleen (18).

C. Carcinogenic Potential

- In a group of 59 mice dermally treated twice a week for up to 569 days with a 20% lead naphthenate solution in benzene, one renal carcinoma, four renal adenomas, and seven benign skin tumors were observed (1,2). No control group was included. IARC reviewed this study and concluded: "Although indicative of a carcinogenic effect of lead naphthenate on the kidney, these results cannot be evaluated, since no control mice were painted with the benzene vehicle alone" (26).

D. Mutagenic Potential

- Lead naphthenate was not mutagenic in the Ames Salmonella test conducted with five strains of bacteria (TA1535, TA1537, TA1538, TA98, and TA100), both in the presence of S-9 activation (rat and hamster liver) and in its absence (3).

- Lead naphthenate was not mutagenic in the standard Ames Salmonella typhimurium test (15).

- Gulfmill E.P.S., a grease which contains 1.5% lead naphthenate, was tested in the mouse embryo cell transformation assay and the mouse lymphoma forward mutation assay. In the mouse lymphoma assay, Gulfmill E.P.S. did cause a significant increase in the mutant frequency in the presence of S-9 metabolic activation. In the absence of S-9, the results are considered equivocal. Equivocal results were also obtained in the cell transformation assay (9).

E. Developmental and Reproductive Toxicity

- No information is available.

F. Metabolism

- A three- to five-fold increase was found in deposition of lead in the hair of rats administered a 1% lead naphthenate solution daily for four weeks. The major portion of the lead was excreted in the feces. Analysis of the lead content of the urine showed the peak urinary excretion being obtained on the first day after administration. The ratio of urinary to fecal lead averaged approximately 1:100. Approximately 40% of the ingested lead was excreted within three days (20).

- An investigation was performed on technicians regularly dealing with lead naphthenate containing lubricants to explore what extent they had absorbed the lead. The degree of absorption was evaluated by measuring the lead content of the blood and delta-aminolevulinic acid (ALA) concentration in the urine. Of the 104 persons examined, 12 showed blood leads greater than 40 ug/dL. Thirteen had an ALA concentration exceeding the normal value of 5.4 mg/L. From these facts it may be deduced that the periodic determination of ALA excretion in the urine and of the blood lead content is of no use for the early detection and evaluation of the individual degree of exposure to lead in persons working with lead-containing oils (22).

G. Biochemical Studies

- No information is available.

H. Human Exposure

- Lead pollution was evaluated in 216 workers employed in automobile garages. Increased lead levels were found in 59% with 9% having blood lead levels greater than 80 ug/dL. Raised lead levels were maximal among diesel mechanics who were exposed to lubricants containing lead naphthenate. Skin absorption may have occurred based on the skin damage observed in these mechanics (4).

I. Epidemiology

- An occupational health examination was made of 26 employees in a coating and resin plant. The plant inventory consists of a broad spectrum of organic and inorganic chemicals. Lead naphthenate use was considered moderate (> 100 and < 1000 pounds per year). A review of the medical findings reveals no evidence of an unusual prevalence of diseases of the CNS, kidney, liver, the blood forming organs, or the skin (21).

J. Aquatic/Environmental Studies

- No information is available.

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