ADME NTP Study S0248 Lead oxide

The contract laboratory used lead (II) oxide for the test article.
Sex/Species: adult male Fischer 344 (F-344) rats.
Vehicle: dosed feed, NRC-AIN-76A powder feed.

CASRN 1317-36-8

No radiolabel was used. Lead in feed was analyzed by an Inductively Coupled Argon Plasma Emission Spectrometer (220.35 nm). Blood samples and femurs were analyzed by a Graphite Furnace Atomic Absorption Spectrometer (283.3 nm).

Studies Performed:

- Animals were exposed to dosed feed with 0, 10, 30, or 100 ppm lead oxide for 30 days (n = 10 per group). Blood and bone (femur) was analyzed for lead on Day 30 and urine for delta-aminolevulinic acid (ALA) on Day 23.

This test article was one of four lead compounds tested together to determine the bioavailability of different chemical forms of lead. The other three test articles were lead (II) acetate, lead (II) sulfide, and an Alaskan lead ore concentrate (NTP studies S0195, S0265, and S0375, respectively).

All four of the test articles were sieved in an 8 inch 400 mesh US Standard Sieve. The fraction of lead oxide that passed through the sieve (-400) was used in the study. The assay value for lead oxide was 93.0 ± 3.3% lead by weight. No significant differences were found in food consumption as a function of dose levels for any of the test chemicals.

Analysis of blood samples taken immediately prior to dosing and at the end of the dosing period showed substantial contamination of a significant number of the samples. For this reason, no conclusions can be made from the blood lead data (data not shown).

On exposure day 23, each rat was transferred to an individual metabolism chamber for collection of urine and were kept there for 6 hours without food and water. They were then returned to their regular chambers. This procedure did not provide sufficient urine from several animals for reliable ALA determination. For later lead studies, this procedure was changed.

Table 1

Concentration of ALA in Urine After
23 Days of Ingesting Lead Oxide in Feed[a,b]

Controls (0 ppm)		10 ppm Lead		30 ppm Lead		100 ppm Lead	
Animal No.	ALA (μg/mL)	Animal No.	ALA (μg/mL)	Animal No.	ALA (μg/mL)	Animal No.	ALA (μg/mL)
1B	c	11B	c	21B	57.5	31B	39.5
2B	21.1	12B	c	22B	c	32B	61.5
3B	12.5	13B	11.2	23B	28.5	33B	26.4
4B	c	14B	18.6	24B	25.5	34B	67.0
5B	8.8	15B	c	25B	c	35B	106.9
6B	c	16B	13.1	26B	15.5	36B	c
7B	10.4	17B	16.1	27B	27.6	37B	c
8B	14.4	18B	28.7	28B	13.6	38B	70.2
9B	16.3	19B	c	29B	15.1	39B	102.1
10B	10.6	20B	20.5	30B	31.0	40B	53.3
Mean	**13.4**		**18.0**		**21.0**		**65.9**
SD	4.2		6.3		7.0		27.9

Controls	Spiked Level	Found
1	4 μg/mL	2.4 μg/mL
2	10 μg/mL	9.4 μg/mL
3	40 μg/mL	40.6 μg/mL

[a] ALA - δ-amino levulinic acid.
[b] Data shown are averages of duplicate determinations for each sample.
[c] Insufficient quantity of urine obtained for analysis.

Table 2

Uptake of Lead in Rat Femurs After 30 Days of Ingesting Lead Oxide in Feed

Dose Level: 0 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
1B	304.8	0.3190	0.00	0.00
2B	284.7	0.2690	0.00	0.00
3B	313.6	0.4420	0.00	0.00
4B	294.0	0.3412	0.00	0.00
5B	300.6	0.3086	0.00	0.00
6B	331.2	0.3398	0.01	0.03
7B	326.6	0.3720	0.02	0.05
8B	302.2	0.3699	0.00	0.00
9B	297.6	0.2998	0.03	0.11
10B	344.4	0.3728	0.00	0.00
Mean	**310.0**	**0.3434**	**0.01**	**0.02**
SD	17.7	0.0462	0.01	0.03
CV	5.7	13.46	174.0	181

Dose Level: 30 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
21B	305.7	0.3532	12.15	34.4
22B	319.2	0.3456	15.97	46.2
23B	305.2	0.3164	19.49	61.6
24B	329.4	0.3314	16.44	49.6
25B	347.9	0.3775	21.82	57.8
26B	331.0	0.3815	11.25	29.5
27B	298.9	0.3287	11.73	35.7
28B	312.1	0.3569	10.53	29.5
29B	329.5	0.3471	7.01	20.2
30B	334.0	0.4017	7.15	17.8
Mean	**321.3**	**0.3540**	**13.53**	**38.2**
SD	14.8	0.0251	0.36	14.3
CV	4.6	7.077	2.64	37.3

Dose Level: 10 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
11B	309.9	0.4717	8.30	17.6
12B	324.7	0.3440	4.71	13.7
13B	333.8	0.3588	6.67	18.6
14B	340.4	0.3582	7.84	21.9
15B	325.6	0.3506	6.38	18.2
16B	318.6	0.2571	2.49	9.7
17B	321.6	0.4044	5.82	14.4
18B	316.3	0.3490	2.62	7.5
19B	321.6	0.3373	5.33	15.8
20B	351.9	0.3981	4.10	10.3
Mean	**326.4**	**0.3629**	**5.4**	**14.8**
SD	11.8	0.0523	1.9	4.3
CV	3.6	14.42	34.7	29.2

Dose Level: 100 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
31B	311.3	0.3855	68.62	178
32B	305.3	0.3689	70.46	191
33B	305.6	0.3621	27.70	76.5
34B	302.1	0.3517	52.76	150
35B	296.7	0.3853	45.08	117
36B	335.9	0.3492	90.09	258
37B	311.0	0.3182	76.69	241
38B	317.0	0.3527	37.39	106
39B	328.9	0.3319	57.09	172
40B	288.3	0.3281	44.95	137
Mean	**310.2**	**0.3534**	**57.1**	**162.7**
SD	13.5	0.0217	18.3	54.7
CV	4.4	6.152	32.1	33.6

Table 3

Correlations of Femur Pb Uptake with Dose

Compound	Regression Equation[a,b]	Correlation Coefficient (r^2)
Lead Acetate	$[Pb]_{femur} = 2.64 \times Dose + 1.24$	0.9938
Lead Oxide	$[Pb]_{femur} = 1.64 \times Dose - 3.53$	0.9953
Lead Sulfide	$[Pb]_{femur} = 0.10 \times Dose + 0.54$	0.9626
Alaskan Ore Concentrate	$[Pb]_{femur} = 0.12 \times Dose + 2.40$	0.8733

[a] Dose in μg Pb/g feed; $[Pb]_{femur}$ in μg Pb/g femur (fresh weight).
[b] Slopes of the regression equations for lead acetate and lead oxide studies were statistically different from each other and from those of the other test compounds. Slopes of the regression equations for lead sulfide and Alaskan lead ore concentrate were not statistically different from each other.