ADME NTP Study S0265 Lead sulfide

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

CASRN 1314-87-0

No radiolabel was used. Lead in feed was analysed by an Inductively Coupled Argon Plasma Emission Spectrometer (220.35 nm). Blood samples and femurs were analysed 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 sulfide 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) oxide, and an Alaskan lead ore concentrate (NTP studies S0195, S0248, and S0375, respectively).

All four of the test articles were sieved in an 8 inch 400 mesh US Standard Sieve. The fraction of lead sulfide that passed through the sieve (-400) was used in the study. The assay value for lead sulfide was 80.2 ± 6.8% 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 Sulfide 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)
1C	5.4	11C	4.7	21C	7.2	31C	5.0
2C	3.5	12C	1.7	22C	c	32C	1.1
3C	6.6	13C	2.9	23C	17.1	33C	c
4C	5.1	14C	c	24C	c	34C	c
5C	c	15C	1.0	25C	8.4	35C	4.2
6C	c	16C	c	26C	0.9	36C	1.4
7C	7.7	17C	4.7	27C	1.5	37C	0.4
8C	4.6	18C	9.7	28C	2.7	38C	6.0
9C	16.2	19C	8.1	29C	3.7	39C	3.8
10C	c	20C	1.3	30C	1.6	40C	1.2
Mean	7.0		4.3		5.4		2.9
SD	4.3		3.2		5.5		2.1

Controls	Spiked Level	Found
1	10 μg/mL	12.8 μg/mL
2	20 μg/mL	19.7 μg/mL
3	40 μg/mL	40.8 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 Sulfide in Feed

Dose Level: 0 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
1C	347.0	0.3811	0.06	0.17
2C	304.4	0.3423	0.13	0.39
3C	341.9	0.3759	0.00	0.00
4C	345.7	0.3641	0.04	0.10
5C	345.9	0.4007	0.01	0.03
6C	289.1	0.3117	0.00	0.00
7C	338.5	0.3632	0.03	0.07
8C	370.7	0.4032	0.03	0.07
9C	358.7	0.3993	0.16	0.40
10C	346.8	0.3827	0.24	0.62
Mean	**338.9**	**0.3724**	**0.07**	**0.19**
SD	23.0	0.0272	0.08	0.20
CV	6.8	7.3099	109.3	108.6

Dose Level: 30 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
21C	388.0	0.3717	0.59	1.58
22C	325.0	0.3494	0.46	1.31
23C	364.3	0.3924	0.49	1.26
24C	304.0	0.3276	1.95	5.96
25C	330.7	0.3783	0.78	2.06
26C	333.6	0.3386	0.24	0.72
27C	325.4	0.3407	1.20	3.53
28C	329.0	0.3367	0.67	2.00
29C	365.3	0.3801	0.63	1.67
30C	327.8	0.3268	2.02	6.19
Mean	**339.3**	**0.3542**	**0.90**	**2.6**
SD	23.8	0.0229	0.59	1.9
CV	7.0	6.4562	65.2	70.8

Dose Level: 10 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
11C	316.8	0.3616	0.95	2.62
12C	337.3	0.3787	0.51	1.34
13C	372.2	0.3825	1.13	2.96
14C	364.7	0.3708	0.57	1.53
15C	356.8	0.4077	0.64	1.56
16C	356.1	0.3644	0.30	0.83
17C	317.9	0.3170	3.07	9.69
18C	355.1	0.3774	0.66	1.76
19C	366.5	0.3782	0.33	0.86
20C	327.0	0.3653	1.36	3.73
Mean	**347.0**	**0.3704**	**0.95**	**2.7**
SD	19.6	0.0217	0.78	2.5
CV	5.6	5.8583	81.6	92.8

Dose Level: 100 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
31C	325.1	0.3255	2.41	7.4
32C	381.9	0.3963	3.08	7.8
33C	326.1	0.3582	2.03	5.7
34C	306.1	0.3708	6.64	17.9
35C	323.9	0.4060	4.06	10.0
36C	354.2	0.3900	8.27	21.2
37C	349.1	0.3965	4.92	12.4
38C	342.6	0.4079	5.30	13.0
39C	355.0	0.4347	1.67	3.9
40C	355.6	0.3792	3.30	8.7
Mean	**342.0**	**0.3865**	**4.17**	**10.8**
SD	20.7	0.0286	2.01	5.2
CV	6.1	7.4049	48.3	47.8

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.