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LITERATURE SURVEY

"Potential Hazards of Ingesting Metal Containing Paints"

by

The Department of Environmental Health
University of Cincinnati Medical School
Cincinnati, Ohio

for

The National Paint and Coatings Association
Washington, D. C.

5386

December 1972

Co + Cd + Be + Pb + Hg + Cu + Sb - ? Ni + ? Cr - ?

University of Cincinnati Medical Center

3223 Eden Avenue
Cincinnati, Ohio 45219

DEPARTMENT OF ENVIRONMENTAL HEALTH
KETTERING LABORATORY
(513) 872-5700

January 4, 1973

Mr. Royal A. Brown
Technical Director
National Paint and Coatings
Association
5100 Rhode Island Avenue, N.W.
Washington, D. C. 20005

Dear Mr. Brown:

Enclosed is the copy of the preliminary literature survey on the "Potential Hazards of Ingesting Metal Containing Paints" carried out for the National Paint and Coating Association by this Department.

As you can see, the effort necessary was larger than originally planned. I hope it serves its purpose well. If the report is to be reprinted or widely circulated, it will need to be more carefully edited and retyped. Please call on me if you have any questions, or when you plan to come to Cincinnati to discuss the report.

Sincerely yours,

Stanley E. Gross

Stanley E. Gross, Ph.D.
Associate Professor of
Environmental Health
(Toxicology)

SEG:np

Enc.

Potential Hazards of Ingesting Metal Containing Paints

A preliminary literature
survey carried out for the

National Paint and Coating Association

Washington, D. C.

by

The Department of Environmental Health
University of Cincinnati
Stanley B. Gross, Ph.D.
Project Director
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December, 1972

Potential Hazards of Ingesting Metal Containing Paints

by Stanley B. Gross, Ph.D.

I. Introduction

Recent concerns over the hazards to children of ingesting leaded paints has prompted a ban on the use of such paints on children's toys and appliances and for interior use. The National Paint and Coatings Association (NPCA), concerned with potential dangers of other metallic constituents, as well as lead, has asked the University of Cincinnati's Department of Environmental Health to carry out a preliminary literature survey on the toxicological significance of metal compounds used by the paint industry, with special concern for hazards by ingestion.

Table 1 contains a list of the specific compounds provided by NPCA which were evaluated. The percentages of these compounds used in paints are found in Section III and in the Summary (Section IV). The search was based on materials readily available within the files of the Kettering Library rather than a search of the new literature. Many more references were available in the Library than could be used for the present survey.

Table 1. Compounds of specific interest provided by the National Paint and Coatings Association.

- Antimony Oxide
- Nickel-Antimony Titanate
- Barium Sulfate
- Barium Meta Borate
- Lithopone (30% Zinc Sulfide - 70% Barium Sulfate)
- Cadmium Lithopone
- Cadmium Selenide
- Cadmium-Barium Soaps (Stabilizers)
- Chromium Oxide
- Lead and Zinc Chromates
- Cobalt Naphthenate and other metallo-organic soaps
- Cobalt Nickel Titanate
- Copper Oxide
- Copper Phthalocyanine
- Copper Naphthenate and other metallo-organic soaps
- Copper Metal
- Basic Lead Carbonate
- Basic Lead Silicate
- Lead Chromates
- Lead Oxides
- Lead Silico-Chromate
- Lead Naphthenate and other metallo-organic soaps
- Lead Metal
- Phenyl Mercuric Acetate, Phenyl Mercuric Oleate and other metallo-organic compounds
- Mercury Cadmium Lithopone
- Nickel Titanate
- Cadmium Selenide Pigments
- Strontium Chromate
- Tri-butyl tin oxide
- Other tin organo compounds
- Aluminum Silicate
- Aluminum Oxide and Hydroxide
- Aluminum Stearate
- Aluminum Metal
- Borates (Barium meta-borate, sodium tetraborate, etc.)
- Boron tri-fluoride
- Calcium carbonate
- Calcium oxide
- Calcium Naphthenate and other metallo-organic soaps
- Lithium hydroxide
- Lithium Naphthenate
- Magnesium Silicate
- Magnesium Aluminum Silicate
- Magnesium Oxide
- Manganese Dioxide
- Manganese Naphthenate and other metallo-organic soaps
- Lead Molybdate
- Zinc Molybdate
- Titanium Dioxide (commercial grades)
- Titanates (Nickel, Antimony, Tungsten)
- Zinc Oxide
- Zinc Stearate
- Lithopone (30% Zinc Sulfide - 70% Barium Sulfate)
- Zinc Naphthenate and other metallo-organic soaps
- Zinc Metal
- Zirconium Naphthenate and other metallo-organic soaps
- Zirconium Oxide

0007-SWP-036834

This report is divided into a brief summary of body metals and their absorption from the gastrointestinal tract, a review of the specific compounds by elemental classes, a summary, and recommendations.

II. Absorption of Metals

Metals in the Body

There is an extensive literature on the role of metals in biological systems. Bowen (5), Lee(37), and the numberous articles by Schroeder and Tipton appearing in the section on References provide an overview of body metals; Browning (6), Gefafer (10), and Stokinger (22) provide recent overview of the toxicity of metals.

The essential bulk metals of the body -- calcium, potassium, sodium and magnesium -- comprise 1.5, 0.2, 0.15 and 0.05% of the body weight, respectively. The remainder of the body metals (the trace metals) make up less than one percent of the total body weight (12). Many trace metals are essential in only milligram and microgram quantities. These metals are important in neuromuscular function, in acid-base balance, in structure and as activators or constituents of many of the body's enzymes.

According to Schroeder's publication in 1960 (25), trace metals found in man may be divided into four groups: 1) metals considered to be essential for mammals, in that the requirements for growth have been established, deficiency

states discovered or essentially inferred as cofactors for certain purified metalloenzymes -- manganese, cobalt, copper, zinc, and molybedenum; 2) metals ubiquitous in plant and animal tissues with suspected metabolic functions but with essentialities unproven -- rubidium, boron, barium, strontium, vanadium, chromium (now considered essential), nickel and aluminum; 3) metals without known functions, believed to be contaminants -- silver and lead; and 4) metals usually not detected in infants but apparently acquired and accumulated as environmental contaminants -- cadmium, tin, titanium and in some locations, bismuth, gold and gallium (rarely).

Excesses of essential or nonessential metals are toxic by inhibiting the absorption of essential metals, by interfering with metallic enzyme activators, by replacing metals in metallo-enzymes or by direct action on non-metallic biochemical systems.

Absorption of Paint Metals

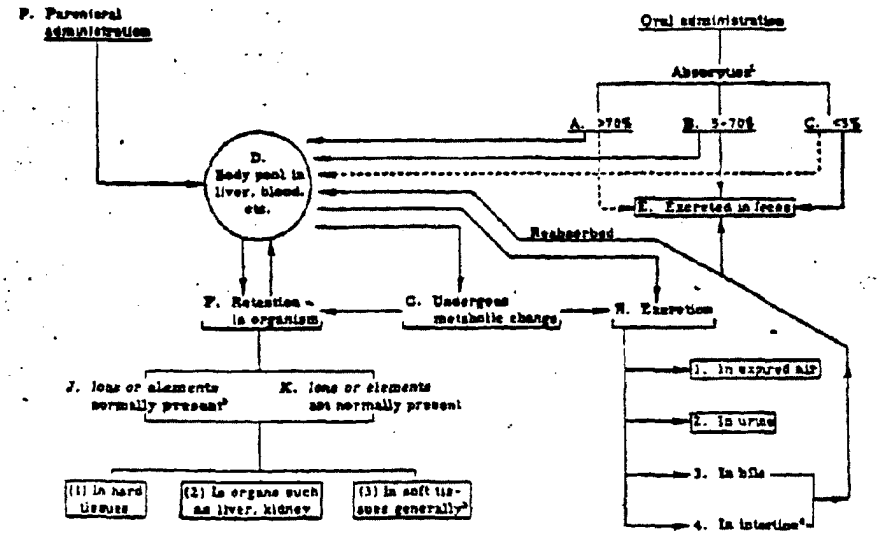
There is a large literature dealing with gastro-intestinal tract anatomy, physiology and biochemistry. The reader is referred to such texts as Kimber et al. (1) and Wilson (2) for general information on intestinal absorption and to Skoryna and Waldron-Edward (3) for a discussion of the intectinal absorption of specific metals.

Figure 1 and Table 2, Pathways for Mineral Metabolism, taken from Altman and Dittner (31), summarize the absorption and disposition of many metals (and non-metals). This information is derived from the literature cited by Altman and Dittner and applies primarily to laboratory animals under experimental conditions. These results are not always consistent with data for humans, such as those data of Tipton and Stewart (24) who carried out balance studies for 22 elements on several individuals. Two of these subjects were followed for 347 days.

Absorption of metals from the alimentary tract is potentially complex. It involves the grinding action of chewing, the mixing due to the physical action of peristalsis, the chemical interactions with saliva, acid gastric juices, alkaline bile, pancreatic and intestinal juices, the potential changes (metabolism) by microorganisms and the interactions of metals with food digests (chelating agents). Other factors are the chemical form of an element, its concentration, its molecular size, its solubility in the different fluids of the intestinal tract and, ionization at the various pH levels. Specie, sex and age differences may also be important.

Figure 1. Pathways of mineral metabolism. Diagram for Table 2. Taken from Altman and Dittner (31).

DIAGRAM FOR TABLE 56



/1/ Percent absorption from oral administration has in some cases been rather arbitrarily classified, since the extent of absorption may depend on the amount administered and on the presence or absence of food residues in the digestive tract. /2/ Some trace elements with no known function also included. /3/ Primarily muscle, skin, and extracellular fluids. /4/ Other than in the bile, or by a route not definitely established.

Table 2. Pathways of mineral metabolism. Taken from Altman and Dittner (31)

The course, or courses, of various ions during metabolism can be located in the diagram (at left) by tracing the combination of letters and numbers accompanying each ion (columns B and C below). Observations were made on a wide variety of mammalian species. Ions were administered in the form of simple soluble compounds or metallic oxides, unless otherwise specified. Underscoring indicates radioactive elements, or that data were obtained at least in part from studies using radioactive isotopes. Different isotopes of the same element may show different tissue predilections, but there is usually no difference in their absorption or route of excretion. "Plus" symbols indicate valence states to which data apply. Other Known Pathways (column C) are listed, so far as possible, in order of decreasing importance.

	Ion	Principal Oral Pathways[a]	Other Known Pathways	Reference
	(A)	(B)	(C)	(D)
		Cations[d]		
1	Actinium	CE	PDFK(1,2)	10
2	Aluminum	CE	PDH2, PDH3, PDFJ(2)	40,91,93
3	Americium	CE	PDH4, PDFK(2,1), PDH2	88,102
4	Antimony+++	BE, BDH2	BDFK(2,3), BDH4	31,34,40,93
5	Arsenic+++	BE, BDH2	BDFK(2,3), BDH4	16,40,54,58,93
6	Barium	BE, BDH4	BDFK(1), BDH2	12,36,89,93,102
7	Beryllium	CE	PDFK(1,3,2), PDH2, PDH4	83,93
8	Bismuth+++	CE	PDFK(2), PDH4, PDH2	40,57,93
9	Cadmium	CE	PDFK(2,3,1), PDH4, PDH2	20,23,48,78,93,110
10	Calcium	BE, BDFJ(1)	BDH4, BDH3, BDH2, BDFJ(3)	3,19,40,75,92,97,103,110,111
11	Cerium[b]	CE	PDFK(2,1), PDH3, PDH2	23,24,40,46,94,102
12	Cesium	ADH2	ADH3, ADH4, ADFJ(3)	36,52,71-74,90,93
13	Chromium+++	CE	PDH2, PDH4, PDFK(2,1)	23,25,50,106
14	Cobalt++	BE, BDH2	BDH3, BDH4, BDFJ(2)	5,17,19,40,56,93,110
15	Copper++	BE, BDH3	BDH2, BDFJ(2)	19,40,64,93,110
16	Curium	Probably CE[c]	PDFK(2,1), PDH4, PDH2	86,102
17	Dysprosium[b]	----------	PDH3, PDFK(1)	24
18	Erbium[b]	----------	PDH3, PDFK(1,2)	24
19	Europium[b]	CE	PDH3, PDH2, PDFK(1,2)	24
20	Francium	Probably ADH2[c]	PDFK(2,3)	76
21	Gadolinium[b]	----------	PDH2, PDH3, PDFK(1,2)	24
22	Gallium	CE	PDH2, PDFK(1,2), PDH4	22,53,93
23	Germanium	ADH2	ADH4, ADFK(2)	93
24	Gold+++	CE	PDFK(2), PDH2, PDH4	34,40,79,93
25	Hafnium[b]	----------	PDFK(2,1), PDH2, PDH4	47,93
26	Holmium[b]	----------	PDH3, PDFK(1,2)	24
27	Indium	CE	PDFK(3,1,2), PDH4, PDH2	23,39
28	Iridium	CE	PDH2, PDH4, PDFK(3,2,1)	23
29	Iron++	CE	PDH4, PDFJ(2)	19,40,65,93,110,111
30	Lanthanum[b]	CE	PDH2, PDH3, PDFK(2,1)	13,23,24,36,40,93,95,102
31	Lead++	BE, BDH4	BDH2, BDFK(1,3,2)	1,9,23,34,35,40,57,82,93
32	Lithium	ADH2	ADH4, ADFJ(3,2)	30,36,81,93
33	Lutetium[b]	----------	PDH3, PDFK(1)	24
34	Magnesium	BE, BDH2	BDH3, BDFJ(1,2,3)	2,40,91,93,110
35	Manganese++	CE	PDH3, PDH4, PDFJ(2,3)	6,19,28,40,60,66,93
36	Mercury++	BE, BDH2	BDFK(1,2,3), BDH3, BDH4	23,40,93
37	Neodymium[b]	Probably CE[c]	PDH2, PDFK(2,1), PDH3	23,24,38,40,93
38	Neptunium	CE	PDFK(3)	36
39	Nickel++	BE, BDH2	BDH4, BDFJ(2)	5,35,40,93,98,106,110
40	Niobium[b]	CE	PDH2, PDH4, PDFK(2,1,3)	13,23,36,80,102
41	Palladium	Probably CE[c]	PDH2, PDH4, PDFK(2)	23,40,67
42	Platinum	CE	PDH2, PDH4, PDFK(2,3,1)	23,40
43	Plutonium[b]	CE	PDFK(1,2), PDH4, PDH2	11,29,36,84,89,102,109
44	Polonium	CE	PDFK(2,1,3), PDH4, PDH2	27,44,93,96,102

/a/ Ions may be considered to follow the same pathways when given parenterally. /b/ Because of inadequate information, no pathways have been listed for berkelium, californium, einsteinium, fermium, and mendelevium. /c/ Usually given as soluble examples. /d/ As judged from the position of the element in the periodic table, or on solubility at neutral pH values.

continued

Table 2. Continued

	Ion	Principal Oral Pathways[a]	Other Known Pathways	Reference
	(A)	(B)	(C)	(D)
		Cations		
45	Potassium	ADH3	ADFJ(3.2), ADH3, ADH4	18,19,40,71,73,103
46	Praseodymium[b]	CE	PDH2, PDFK(2,1), PDH3	24,36,40
47	Promethium	CE	PDH2, PDFK(2,1), PDH3	24,36,102
48	Protactinium	Probably CE[c]	PDFK(1)	88
49	Radium	BE, BDFK(1,2)	BDH4, BDH2	27,45,75,93,97,102
50	Radium D	Probably BE, BDH2[c]	PDH2, PDH4, PDFK(1)	9,70
51	Rhodium	CE	PDFK(3,2,1), PDH2, PDH4	23
52	Rubidium	ADH2	ADFJ(3,2), ADH3, ADH4	68,71
53	Ruthenium	CE	PDH2, PDH4, PDFK(3,1,2)	23,100,101
54	Samarium	CE	PDH2, PDFK(2,1), PDH3	23,40
55	Scandium	Probably CE[c]	CDH2, CDFJ(1,3)	4
56	Selenium	ADH2	ADGH1, ADFK(2,3), ADH4	61,62,93
57	Silver	CE	PDH3, PDFK(2,3), PDH2, CDGFK[d]	40,87,93,119
58	Sodium	ADH2	ADFJ(3,1,2), ADH3, ADH4	19,40,91,93
59	Strontium	BE, BDFK(1)	BDH2, BDH4, BDH3	3,36,45,75,92,102,103
60	Tantalum	CE	PDH2, PDH4, PDFK(2,1,3)	23,24
61	Technetium	.....	PDH2, PDH4, PDFK(3,2,1)	23
62	Tellurium[++++]	BE, BDGH2	BDGH3, BDGH1, BDGFK(2)	36,93,102
63	Terbium[b]	CE	PDH2, PDH3, PDFK(1,2)	24
64	Thallium	BE	BDH4, BDFK(3,1,2), BDH2	40,89,93
65	Thorium	CE	PDFK(2,1), PDH4, PDH2, PDH3	36,85,93,102
66	Thulium	CE	PDH2, PDH3, PDFK(1)	24
67	Tin[++]	BE, BDH2	BDFJ(3,2), BDH4, BDH3	40,93,118
68	Tin[++++][e]	BE, BDH2	BDH4, BDFJ(1,3,2)	23
69	Titanium	Probably CE[c]	CDFJ(2)	93
70	Uranium[++++]	.....	BDFK(2)	102
71	Uranium[++++++]	BE, BDH2	BDFK(1,2)	21,40,93,102
72	Ytterbium[b]	.....	PDH3, PDFK(1,2)	24
73	Yttrium	CE	PDFK(1,2), PDH2, PDH4	13,24,32,36,46,84,102,109
74	Zinc	CE	CDH4, CDFJ(2,3), CDH2	33,40,60,77,93,102-105,118
75	Zirconium	CE	PDFK(1,3)	13,36,80,102
		Anions[f]		
76	Astatide	Probably A[c]	PDFK(3), PDH2, PDH4	37
77	Bicarbonate	ADH1, ADH2, ADH3	ADH4, ADFJ (all tissues)	93
78	Borate	ADH2	.....	40,93
79	Bromate	ADH2	ADG (to bromide)	41,93
80	Bromide	ADH2	ADH3, ADH4, ADFJ(3)	34,93
81	Chlorate	ADH2	.....	40,93
82	Chloride	ADH2	ADH3, ADH4, ADFJ(3,1,2)	91,93
83	Chromate	BDH2	BDH4, BDGH2, BDGH4, BDGFK(2)	40,63,93,106
84	Cyanide	ADH2	ADH1, ADG (to SCN^-)	93
85	Ferrocyanide	ADH2	.....	48,49,93
86	Fluoride	BDH2	BDFJ(1,3), BDH4	60,91,93
87	Hypophosphite	ADH2	.....	93
88	Iodate	ADG (to iodide)	PDH2	93
89	Iodide	ADH2	ADFJ(3,2), ADH3	93
90	Molybdate	BDH2	BDFJ(2,3,1)	7,15,24,35,40,99,108
91	Nitrate	ADH2	ADFK(3)	93
92	Nitrite	ADG (to nitrate)	.....	93
93	Osmate	.....	PDH2, PDH4, PDFK(3,2,1)	23
94	Oxalate	ADH2	.....	93
95	Perchlorate	ADH2	.....	41
96	Permanganate	CE (reduced to MnO_2)	.....	41
97	Perrhenate	CE	PDH2, PDFK(3)[g], PDH4	23,42
98	Phosphate	BE, BDH2	BDFJ(1,2,3), BDH3, BDH4	19,93
99	Silicate	BE, BDH2	BDFJ(2)	34,35,42,91,93
100	Sulfate	BE, BDH2	BDH3, BDH4, BDG	19,26,31

[a] Ions may be assumed to follow the same pathways when given parenterally. [b] Usually given as soluble complex. [c] As judged from the position of the element in the periodic table, or on solubility at neutral pH values. [d] Skin. [e] Because of inadequate information, no pathways have been listed for cyanide, ferrocyanide, and periodate. [f] As judged from solubility at neutral pH values.

continued

Toxicity and Hazard

The term "toxicity" as used in this report, refers to the innate ability of a material to induce harm once inside the body. "Hazard" refers to the ability of a toxic material to be absorbed into the body where it might effect its toxic action. A highly toxic material, for example, which cannot be absorbed appreciably from the gastrointestinal tract would not be a significant hazard. The mere presence of a toxic material at a low concentration inside the body also may not constitute a significant hazard. A toxic substance to be considered a hazard, should cause measurable adverse effects (such as irritation, growth impairment, disease, etc.) when used as intended and at levels approximating intended use. Usually safety factors are applied when setting standards.

Table 3, taken from Spector (18), presents commonly used terms that are associated with acute exposures by various routes. These terms are used in the body of this report in similar fashion.

III. Compounds by Elemental Class

This section considers the toxicity and hazards of the specific compounds by elemental classes. The original list suggested by NPCA is found in the Introduction. An expanded alphabetical listing of these compounds can be found in the Summary.

Table 3. Combined tabulation of toxicity classes* taken from page 4 of Spector (18).

Toxicity Rating	Commonly Used Term	LD_{50} Single Oral** Dose Rats	Inhalation 4 hr Vapor Exposure Mortality 2/6-4/6 Rats	LD_{50} Skin Rabbits	Probable Lethal Dose for Man
		Various Routes of Administration			
1	Extremely toxic	1 mg or less/kg	<10 ppm	5 mg or less/kg	A taste, 1 grain
2	Highly toxic	1-50 mg	10-100	5-43 mg	1 teaspoon 4 cc
3	Moderately toxic	50-500 mg	100-1000	44-340 mg	1 ounce 30 gm
4	Slightly toxic	0.5-5 g	1000-10,000	35-2.81 g/kg	1 pint 250 gm
5	Practically non-toxic	5-15 g	10,000-100,000	2.82-22.59 g/kg	1 quart
6	Relatively harmless	15 g and more	>100,000	22.6 or more g/kg	>1 quart

* Hodge, H. C., and Sterner, J. H., American Industrial Hygiene Association Quarterly, 10:4,93, Dec 1949

** Standards for intravenous LD_{50} for rats and rabbits may be obtained approximately by dividing the oral toxicity standards for rats by 10.

Since many of the compounds belong to more than one elemental class, they appear listed at the beginning of each class to which they belong, along with the concentrations at which they are used in paints.

References 4 to 26 were used "routinely" for all elements or compounds while the other references generally refer to specific compounds or classes of compounds.

In each section are provided, when available, the following types of information: (a) overall toxicity, estimated from animal and human data obtained primarily from ACGIH (4), Browning (6), Christensen (7), Fairhall (8), Sax (16), Spector (18) and Stokinger (22); (b) body burden data, taken primarily from the ICRP Committee II report (12) and (c) data on absorption and disposition (18, 24, 25) providing an indicator of absorption and excretion rates and the amount of body pools which might assimilate the absorbed metals; (d) acute oral hazards, taken from Christensen (7) and Spector (18), based primarily on animal studies; (e) water supply criteria and standards which describes human chronic oral exposure, primarily taken from McKee and Wolf (13); (f) toxicity data on specific compounds obtained primarily from Christensen (7), Spector (18), Sax (16) and Stecher (14); and (g) oral hazards in paints, which, based on the above information, suggests the degree of potential hazard in using these compounds in paints.

In many cases there are insufficient data available on which to base safe levels of these compounds in paint formulations. Recommendations for studies to obtain this information are presented in Section V, Recommendations.

Aluminum Compounds

Aluminum Metal	0 - 25%
Aluminum Hydroxide	0 - 5%
Magnesium Aluminum Silicate	0 - 25%
Aluminum Oxide	0 - 5%
Aluminum Silicate	0 - 50%
Aluminum Stearate	0 - 10%

There is a considerable literature on aluminum and its health effects. In addition to the "routine" references (4-26), the 1957 review of Campbell et al. (27) of this Department is useful. Dr. John Sorenson, also of this Department, is currently updating the 1957 review.

Aluminum is very abundant in the earth's crust and is widely used in metallurgy, in various chemical industries, and as a therapeutic agent. This element is considered to be nonessential to man and generally of low toxicity once inside the body. In the industrial setting, the oxide (Al_2O_3) is considered only as a nuisance dust. The Threshold Limit Value, TLV, is set at 30 mppcf (4). However, a benign pneumoconiosis

(aluminosis) due to very high levels of dust exposure has been reported. The etiology of the aluminosis is debated (6, 10).

The body contains an estimated 100 mg of aluminum distributed relatively uniformly in most organs in concentrations of approximately 1 ppm, wet weight basis (12). The lungs contain approximately 24 ppm while the skin, ileum, trachea and blood contain 24, 28, 1.8, 2.0 and 0.16 ppm, respectively. The concentration of aluminum in the lungs increases with age in men (26).

The human diet contains 10-150 mg of aluminum per day (26), almost all of which is excreted in the feces. Tipton and Stewart (24) found in two subjects on normal diets averaged over 347 days, daily oral intake of 17 mg each, a fecal excretion of 17 and 15 mg and urinary excretion of 0.87 and 0.72 mg.

Large oral doses of aluminum compounds are necessary to kill or damage experimental animals -- lethal doses (LD's) from 3730 to 4280 mg/kg (18). The species and types of compounds used are important. Spector (18) reported an oral LD50 (lethal dose killing 50% of the animals) for $AlCl_3$ in the rat as 3730 mg/kg $AlCl_3$ while Evenshtein (28) reported a study in which 750 mg $AlCl_3$ administered to a rabbit caused death in two hours. Christensen (7) lists the oral LD50 for aluminum sulfate for the mouse at 770 mg/kg.

There are no standards set for domestic water supplies because of the low level of toxicity of aluminum. Cooking with aluminum utensils can add 70-75 mg to the diet with no apparent harm. In one study (28), one man reported ingesting 264 mg/day for 70 days without ill effect. Rabbits, however, maintained on water with 1400 ppm aluminum developed decreased blood, bone and urine phosphate (13).

Specific Paint Compounds. Aluminum metal dust has been reported to produce contact dermatitis and bronchial asthma (14) and pulmonary fibrosis (16) in industrial use but is not generally regarded as an industrial poison. Aluminum hydroxide is used as a food additive (29) and as an anti-acid with good safety. Aluminum oxide (Alumina) industrially has been associated with pulmonary fibrosis (Shaver's disease), the etiology of which is controversial. Toxicity data on the other compounds were not readily available in the literature.

Oral Hazard in Paint. Based on the poor absorption from the gastrointestinal tract and on the relatively low toxicity of aluminum compounds in man, the specific aluminum compounds under consideration by the paint industry should be safe at the concentrations specified.

Antimony Compounds

Nickel - Antimony Titanate	0 - 15%
Antimony Oxides	0 - 10%

Antimony plays no known essential metabolic role in biological systems and has been known for its toxicity since Roman times (32). This toxicity has been demonstrated in its therapeutic uses as an emetic (potassium antimony tartrate) and for the treatment of human parasitic diseases (schistosomiasis and leishmaniasis), in food poisoning from enameled cooking ware and in accidental and industrial poisonings. Lethal doses by parental routes vary from 3.07 to 4000 mg/kg. Industrial TLV for antimony and its compounds is set at 0.5 mg/m^3. The TLV of the highly toxic hydride of antimony, stibine, is also 0.5 mg/m^3.

Antimony probably exerts its toxic action by reacting with sulfhydryl-containing enzymes, thus interfering with cellular metabolism.

The body is estimated to contain about 90 mg of antimony with tissue levels of 0.05 to 4 ppm, wet weight basis (12). Little appears to be known about normal dietary levels of Sb. Woolrich (30) indicated less than 100 µg Sb per day is contained in the diet. Gastrointestinal absorption is between 5 and 70%, most of which is excreted rapidly in either the urine or the feces (31).

Acute oral LD50 studies for Sb compounds in animals range from 100 to 20,000 mg/kg (7, 18). A lethal dose of antimony potassium tartrate is estimated at 2 mg/kg for man.

There is no permissible level established for domestic water use. Antimony added to the food of rabbits caused progressive increases in both Hb and RBC's and when fed to rats caused an increase in WBC's (6). Antimony fed at 5 ppm over a life time caused a decreased survival and longevity in rats (26).

Specific Paint Compounds. Antimony oxides. The pentoxide was reported to have low toxicity (ip LD50 in rats, 4 gm/kg). Rats tolerated well 4 mg daily, however, both rats and rabbits experienced reduced growth rates on dietary levels of 2% (13). Toxicity information on the tetraoxide or on nickel antimony titanate was not readily available.

Oral Hazard in Paint. Because various antimony compounds have been found to be highly toxic in man and animals, oral hazards of antimony compounds in paints should be adequately evaluated to determine if currently used concentrations in paint are safe.

Barium Compounds

Barium Metaborate	0 - 15%
Barium Soaps	0 - 3%
Barium Sulfate (in lithopone)	0 - 35%
Cadmium-Barium Soaps	0 - 3%
Lithopone	0 - 50%

There is a relatively large literature on barium available in the Department's library, including several recent reviews by Browning (6), Schroeder (33), Miner (34), and Rumyantsev (35).

Barium is relatively abundant in nature. It is nonessential to man and soluble forms are considered highly toxic. Lethal doses range from 4-700 mg/kg depending on the route of administration and species. The industrial TLV is 0.5 mg/m^3 as Ba. Barium stimulates smooth, striated and cardiac muscle and may produce violent peristalsis, arterial hypertension, muscle twitching and cardiac dysfunction. Barium sulfate, used extensively as an x-ray contrast medium, is relatively insoluble and apparently innocuous when ingested. Prolonged inhalation of Ba compounds has been reported to cause a benign form of pneumoconiosis known as baritosis.

Barium behaves similarly to Ca and Sr and is found notably in bone tissue and the aorta, where it is deposited irreversibly (33). Ba presumably can displace Ca to some extent in biological systems by mass action.

The body contains approximately 16 mg of Ba with most of the organs containing levels in ppb range except for bone which contains approximately 1.63 ppm (12). Barium has been shown to accumulate in the lungs with age, apparently due to deposition from inhalation. The diet contains approximately 16 mg/day (26). Tipton and Stewart's (24) individuals' diets contained an average of 0.65 and 0.92 mg/day over 347 days. Excretion averaged 0.69 and 0.88 mg in feces and 0.037 and 0.017 mg in the urine respectively.

Acute oral lethal doses in animals range from 7-9600 mg/kg. Five hundred to 600 mg of a barium compound in man has been reported as fatal (13). The USPHS 1962 water standards for domestic water supplies limits Ba to 1 mg/l based on the toxicity of barium (13).

Specific Paint Compounds. $BaSO_4$ is used as a contrast medium for gastrointestinal x-rays. It is considered innocuous; however, this use is on a short term basis -- usually a single pass through the gastrointestinal tract. Data on humans, especially the young, on a chronic exposure basis are not apparently available. Lithopone has been considered "non-toxic"; however, Sax (16) indicates that hydrogen sulfide can be liberated from lithopone on decomposition by moisture, acid, or heat.

Oral Hazard in Paint. Barium chloride apparently is readily absorbed and is highly toxic to many species (18). Since insoluble barium compounds might form chlorides in the stomach all the barium compounds of concern (soluble or insoluble) used in paints should be adequately evaluated for chronic and short term exposures.

Boron Compounds

Boron Tri-fluoride	0 - 1%
Borates (Barium metaborate	0 - 15%
sodium metaborate, etc)	

The literature on the health effects of boron compounds is relatively limited. Browning (6) and Durocher (38) offer recent reviews of this subject.

Although essential to higher plants, boron is not considered essential to man and has no known metabolic role. Boron and its compounds are considered by Sax (16) as not highly toxic to man. The most common health hazards have been accidental ingestion of household chemicals, such as boric acid or borax, and absorption of boric acid from wounds or burns. The most highly toxic boron compounds are the boranes used in high energy fuels. Lethal parenteral doses of boron compounds range from 20 to over 2000 mg/kg depending on the species, route of administration, and the compound. Industrial TLV's are set at

3, 0.3, 0.1 and 0.01 mg/m^3 for boron trifluorides, decaborane, diborane, and pentaborane, respectively.

Boric acid may produce primary skin irritation and conjunctivitis locally. The ingestion of excessive doses of borates may cause nausea, cramps, convulsions, coma, and other symptoms of distress. Inhalation of the boranes may lead to chest tightness, cough, headache, dizziness, convulsions and unconsciousness.

The body contains approximately 10 mg of boron. Most of the tissues contain sub-ppm quantities except bone which may contain nearly 3 ppm. The diets in Tipton and Stewart's studies (24) contained 1.2 and 11 mg/day with most of the boron being absorbed and excreted in the urine (0.95 and 4.7 mg). Lethal oral doses in animals ranged from 45 to 5140 mg/kg (7, 18). Fifteen to 20 gm of boric acid has been lethal to adults and 506 gm to children. Rats drinking water containing 0.25% boric acid experienced decreased growth rats; however, boron in public drinking water is not generally regarded as a hazard to human beings (13). Concentrations to 30 mg/l of boron in drinking water have been reported as not harmful. Hoskins, however, has recommended a boron limit of 20 mg/l in drinking water (13).

Specific Paint Compounds. Boron trifluoride is highly hazardous by the inhalation route (TVL, 1 mg/m^3). It is highly irritating to mucous membranes. Oral hazard data were not readily available from the references used. Borates. Sodium borate is strongly alkaline and soluble in water. Its oral LD50 for the mouse is 2.0-3.0 gm/kg (38), which can be considered only slightly toxic. Intravenous administration of 0.3 gm/kg of sodium metaborate to the rabbit caused no notable toxic effects.

Oral Hazard in Paint. Orally, the borates are probably relatively non-toxic on a short-term basis; however, inadequate data are available on long-term exposures. Since boron once inside the body can be quite toxic, the oral hazards of these compounds in paint formulations should be more adequately investigated to determine safe levels for paints.

Cadmium Compounds

Cadmium Barium Soaps	0 - 3%
Cadmium Lithopone	0 - 15%
Mercury Cadmium Lithopone	0 - 15%
Cadmium Selenide	0 - 15%
Cadmium Selenide Pigments	0 - 25%
Cadmium Soaps	

There is an extensive and rapidly growing literature on health effects of cadmium and its role in the pollution of our environment. Recent survey articles by Browning (6) and Fasset (39) and extensive reviews by Athanassiadis (40) and Friberg (41) are available.

Cadmium is not widely distributed in nature and finds its way into the biosphere primarily as waste products of technology. Cadmium is considered to be highly toxic to man by any route of administration. Although Cd tends to be deposited irreversibly in the liver and kidneys (metallothionine) as a possible protective storage of the metal, cadmium in toxic levels interferes with the many -SH containing enzymes and many metal-containing enzymes.

Ingestion of cadmium has caused nausea, salivation, vomiting, diarrhea, and abdominal pain. Locally, it is irritating to mucous membranes, produces yellow discoloration of the teeth, and contact dermatitis due to hypersensitization. Inhalation of cadmium fumes may be followed by respiratory irritation, dry throat, metallic taste, chest pain and dyspnea due to bronchitis, pneumonitis and pulmonary edema. Liver, kidneys and bone marrow may be damaged.

Lethal doses in animals range from 2 to 250 mg/kg depending on the chemical form and species (7, 18).

Cadmium fumes at 9 mg/m^3 has caused death in man. The TLV's for Cd are 0.1 and 0.2 mg/m^3 for the oxide fumes and soluble dusts, respectively.

The body is estimated to contain approximately 30 mg of cadmium. Most tissues contain less than 1 ppm except for the kidney (32 ppm), the liver (2.4 ppm), and the pancreas (1.2 ppm). Under normal exposures, Cd accumulates in the kidney with age. The diet contains approximately 25 µg/day, the major portion of which is absorbed and excreted in the urine (42 and 83%) (12, 24).

Acute deaths in animals are seen with oral doses of 70-369 mg/kg. Food poisoning from Cd-plated containers has been reported. One boy died two hours after ingesting 8.7 gm of $CdCl_2$. Limits for domestic water supplies were set at the low levels of 0.05 mg/l by the WHO European/1962 Standards and 0.01 mg/l by the USPHS/1962 Standards organizations because of the highly toxic nature of Cd (13).

Specific Paint Compounds. Most of these compounds listed in Sax (16) and the Merck Index (14) were listed with cross reference to the high toxicity of cadmium and mercury compounds. Lithopone compounds would have added potential hazard due to the possible liberation of H_2S gas (See Barium Compounds above). Cadmium selenide has a low toxicity because of the compound insolubility (14). Cadmium stearate has an oral LD50 of 1225 mg/kg in the rat, giving this a "moderate" toxicity rating.

Oral Hazard in Paint. Because of the highly toxic nature of cadmium in man, cadmium salts should not be used in interior paints or on children's articles without extensive research showing its nonabsorbability from paint formulations, both from short-term and long-term exposures.

Calcium Compounds.

Calcium Carbonate	0 - 70%
Calcium Napthenate	0 - 2%
Calcium Oxide	0 - 15%
Calcium Soaps	0 - 2%

Calcium is the most abundant metal in the earth's crust and is essential to all forms of life. It is also the most abundant divalent metal in the body and is essential for many functions including the activation of many enzymes, neuromuscular irritability, and the structure of bone and teeth. There is a large literature on the roles of calcium in living systems. However, for the purpose of this review, the "routine" references (4-26) provide the primary sources of toxicological information.

Many calcium compounds are used therapeutically and are considered to be relatively non-toxic. Problems of dietary deficiency of calcium have been of more concern to the general population than the toxicity of calcium. On the other hand, industrial exposure to dusts containing

calcium oxide (lime) and calcium arsenate have been of concern -- the oxide because of its irritation to the skin, conjunctiva, cornea and mucous membranes of the respiratory tract and the arsenate because of the arsenic toxicity. The TLV's for these materials are 5 and 1 mg/m^3 respectively.

The body contains about 1050 gm of calcium most of which (99%) is found in the bones. Tipton and Stewart (24) reported 940 and 2300 mg per day of calcium in the diet with only 140 and 230 mg being excreted in the urine, the rest appearing in the feces. The human body requires approximately 0.7 to 2.0 gm of calcium per day as a food element and amounts considerably in excess of these requirements are consumed with the use of hard water without overt adverse effects.

Parenteral and oral lethal doses in animals range from 100 to 25,000 and 15 to 7340 mg/kg respectively depending on the compounds, species and routes of administration (7, 18). Because of its low oral toxicity, the USPHS drinking water standards of 1962 and the WHO European Standards of 1961 do not contain limits for calcium; however, the WHO International Standards of 1958 indicate 75 mg/l as a permissible limit and 2000 mg/l as an excessive limit.

Specific Paint Compounds. Calcium carbonate is used as a nutrient and/or dietary supplement (29), anti-acid and anti-diarrhea agent and is relatively non-toxic. Calcium Oxide is also used as a dietary supplement (29) but is relatively toxic as an industrial dust. In short term studies using calcium naphthenate, Rockhold reported an oral LD50 greater than 6 gm/kg in rats (42). The soap, calcium stearyl-2-lactylate, is used as a food additive and is considered relatively non-toxic.

Oral Hazard in Paints. Based on the fact that relatively high levels of calcium can be safely tolerated in the diet or as oral therapeutic agents in man, the relatively low toxicity of the calcium compounds in question and the probable unabsorbability of these compounds from ingested paint chips, these compounds can probably be considered as only a slight oral hazard in paint formulations.

Chromium Compounds

Chromium Oxides	0 - 15%
Lead Chromate	0 - 25%
Lead Silico Chromate	0 - 25%
Strontium Chromate	0 - 25%

There is an extensive literature on the health aspects of chromium. Browning (6), Sullivan (47) and Smith (48) provide recent overviews for chromium.

Chromium is an essential element involved with glucose and lipid metabolism (an insulin factor). The biologically active form of Cr is not known. Chromium metal itself is relatively inert. Di- and tri-valent chromium compounds are relatively non-toxic; however, the hexavalent forms (chromates and dichromates) are considered highly toxic. Most toxic hazards are from airborne chromium in industrial settings. Cutaneous allergy is not uncommon from hexavalent compounds but are rare from trivalent chromium compounds. Contact with chromates or chromic acid can produce small, painless cutaneous ulcers as well as primary irritation or hypersensitivity. Allergic bronchial asthma has been associated with chromium trioxide fumes. Bronchogenic carcinoma has occurred at an abnormally high rate among chromate workers. Industrial TLV's are 0.1 mg/m^3 for chromic acid and chromates 0.05 mg/m^3 for soluble chromic and chromous salts, and 1 mg/m^3 for metallic chromium and insoluble salts.

The body contains approximately 6 mg of Cr, the bones containing 0.49, the lungs 0.2, the skin 0.33 and the uterus 0.24 ppm. Chromium accumulates in the lungs with age. The daily diet contains approximately 60 ug (26) per day. In Tipton and Stewart's studies (24), 0.20 and 0.29 mg appeared in the diet with 55 and 41% excreted in the urine. Parenterally, lethal doses of various chromium

compounds vary from 0.11 to 6185 mg/kg while acute oral doses vary from 1870-3250 mg/kg (7,18). Rabbits receiving 1.9 gm of $K_2Cr_2O_7$ died within two hours.

Schroeder found the 5 ppm of Cr +3 in the diet of rats to be beneficial. Both the USPHS 1962 and the WHO European 1961 agencies set 0.05 mg/l as a standard for hexavalent chromium in drinking water apparently because of a concern for possible carcinogenicity (13). McKee and Wolf (13), however, question this restrictiveness because of a case of a family which had drunk water containing 25 mg/l of Cr +6 for years (1957 on) with no apparent adverse effects.

Specific Paint Compounds. Chromium oxides. All of the hexavalent oxides are orally toxic, producing gastrointestinal irritation, vomiting and diarrhea, and in experimental animals, renal damage. Oral toxicity data on the other compounds were not readily available from the references used in this survey.

Oral Hazard in Paints. Chromium compounds, especially the hexavalent forms of chromium, have the potential of toxic action at relatively low levels. It is not sufficiently clear from this brief survey what oral hazard would be provided by ingesting the specific compounds to be used in paint formulations. Experimental investigation will probably be necessary to establish acceptably safe levels.

Cobalt Compounds

Cobalt Naphthenate	0 - 1%
Cobalt Nickel Titanate	0 - 20%
Cobalt Soaps	0 - 1%

Cobalt is a relatively rare element, composing about 0.001% of the earth's crust. The toxicity literature on cobalt is relatively limited. The "routine" references (4-26) were used. Stokinger (22) and Browning (6) deal with the general toxicity of cobalt and Valberg (63) discusses the gastrointestinal absorption of cobalt. Cobalt is an essential trace element for man and animals. It is an important constituent of vitamin B_{12} and certain enzymes, and is associated with the production of erythropoietin, and red cell stimulating factor.

Parenteral lethal doses of cobalt compounds in animals vary from 21 to 1400 mg/kg (7, 18). Administration of cobalt salts produces polycythemia. In one case of human poisoning, liver and kidney damage was attributed to cobalt. Metallic cobalt dust and cobalt salts may produce allergic contact dermatitis and corneal irritation. Inhalation of cobalt dust has been associated with gastrointestinal irritation and possible bronchial asthma. The industrial TLV for cobalt metal dust or fume is 0.1 mg/m^3.

The body contains an estimated 3 mg of cobalt with most tissues containing 0.1 ppm or less. Cobalt is

concentrated in bone, liver, kidney and cecum at 0.6, 0.3, 0.2 and 0.26 ppm, respectively. In the studies of Tipton and Stewart (24), the diets contained 300 and 500 µg per day with most of the cobalt being excreted in the feces (48 and 77%).

Oral lethal doses of cobalt range from 0.5 to 1700 mg/kg (7, 18). Excessive oral intake causes nausea and vomiting. Five hundred mg/day for 30 days was lethal for calves and 50 mg/kg was lethal to chicks. Three to 4 mg/day given to children for the treatment of anemia was goitrogenic. The ingestion of 0.1 to 0.25 mg per day does not appear to have any adverse effects whereas single daily doses of 25 mg per day over a period of one week or longer increase the hemoglobin content of blood. McKee and Wolf (13), however, state that maximum safe concentration for cobalt in drinking water cannot be established or estimated on the basis of present knowledge.

Specific Paint Compounds. Cobalt napthenate was found by Rockhold (42) to have an oral LD50 in rats of 3.9 gm/kg. Toxicity or solubility data on the other cobalt compounds were not readily available.

Oral Hazard in Paints. Since relatively low levels of cobalt intake can be toxic to children, appropriate studies to establish safe levels of cobalt compounds in paint formulations should be carried out.

Copper Compounds

Copper Metal	0 - 50%
Copper Naphthenate	0 - 5%
Copper Oxides	0 - 25%
Copper Phthalocyanine	0 - 5%
Copper Soaps	0 - 5%

Copper is an essential element to man in that it is required for the formation of erythrocytes and hemoglobin as well as being an essential part of several proteins: ceruloplasm, tyrosinase, cerebrocuprein, erythrocuprein, cytochrome oxidase, and other proteins. There is a large literature on copper essentiality, biochemistry and toxicity. Scheinberg and Sternlieb (43) and Davenport (68) provided extensive reviews. For more recent reviews see Scheinberg (45), Browning (7), and Van Campen (46).

The toxicity of copper compounds has been known for centuries. Soluble copper salts are strongly irritating to the skin and mucous membranes. Ingestion of excess quantities (copper sulfate) in man has caused vomiting, gastric pain, convulsions, and death (16). Nerve, kidney and liver damage has been recorded. Metal fume fever ("brass chills") results from the inhalation of copper dust or fumes (TLV for fumes, 0.1, and for dusts, 1.0 mg/m^3).

The body contains approximately 100 mg of Cu, concentrated mainly in the liver, brain, kidney, heart and stomach (12). The diet normally contains from 2 to 20 mg per day with most of it being excreted in the feces (24).

Lethal oral doses in animals range from 22-940 mg/kg. Hemolytic anemia has been induced by the therapeutic use of copper sulfate. Sixty to 100 mg in the diet due to heating tea in a copper pot has caused gastroenteritis (13). Three ounces of 1% copper sulfate also caused one case of enteritis. Ten to 30 mg per day in drinking water apparently causes no symptoms; however, because of bad taste problems, USPHS 1962 standards limit copper to 1 mg/liter (13).

Specific Paint Compounds. Copper metal is insoluble in water but soluble in acids and therefore may form absorbable compounds in the stomach. Copper naphthenate, orally administered to rats (42), had an LD50 greater than 6 gm/kg (low toxicity); however, Gefafer (10) describes the naphthenate as an irritant. Copper oxides, used in fungicides, are irritants (10) and are soluble in acid. Copper soaps are generally insoluble in water or acid (19, 20).

Oral Hazard in Paints. Relatively small amounts of absorbed copper can exert a toxic effect on the body. None of the above information is sufficient to assume safety of oral ingestion of copper-containing paints in children, especially for long-term exposures. Therefore, studies should be carried out to establish safe levels for these materials in paints.

Lead Compounds

Lead Carbonate, basic	0 - 60%
Lead Chromates	0 - 25%
Lead Metal	0 - 25%
Lead Molybdate	0 - 15%
Lead Naphthenate	0 - 3%
Lead Oxides	0 - 50%
Lead Silicate, basic	0 - 15%
Lead Silico-Chromate	0 - 25%
Lead Soaps	0 - 3%

Lead is biologically nonessential to man. It has created considerable concern for its possible environmental health effects because of its use in automobile gasolines, paints and many other products. There exists an extensive literature on the biological effects of lead. This literature is regularly reviewed and abstracted in our Department's Lead Abstracts. Several recent reviews

are available, such as the National Academy of Sciences' "Airborne Lead in Perspective" (49), Hammond's "Lead Poisoning: An Old Problem with a New Perspective" (50), and more recently Goyer and Chisolm's lead review (51).

Lead poisoning is one of the most common of occupational diseases. The industrial TLV's (4) for lead as lead, lead arsenate or tetramethyl lead are 0.15 mg/cu. m. and for tetraethyl lead, 0.1 mg/cu. m. Inorganic lead poisoning may produce abdominal pain (colic), constipation, headache, weakness, muscular aches or cramps, loss of appetite, nausea, vomiting, anemia and other signs and symptoms. Lead palsy and lead encephalopathy resulting from industrial exposure is rare but not infrequent in children exposed to lead. Children poisoned by lead may develop mental retardation as well as permanent paralysis and other sequelae. Symptoms of organic lead poisoning are usually confined to the nervous system.

Biochemically, lead interferes with several enzymes involved with the synthesis of hemoglobin which leads to increased urinary excretion of coproporphyrins and delta-aminolevulinic (ALA) acid and decreased blood ALA synthetase and ALA dehydratase. High levels of lead are also associated with hyperglycuria, hyperamino aciduria, hyperphosphaturia and hypophosphatemia. The action of lead on the kidney and on neuromuscular activity is not well understood.

The body is estimated to contain 80 to 120 mg of lead, most of which (over 90%) is stored in bone. Except for bone, most tissues contain 1 ppm or less of lead. The normal adult diet contains approximately 0.3 mg of lead per day, most of which is excreted in the feces. About 10% of the dietary lead is absorbed and excreted in the urine. Lead normally accumulates in bone and other calcified tissue (aorta) with age. Kehoe (52) found in young adults that supplementing normal diets with 0.3 mg of lead (total of 0.6 mg of dietary lead/day) caused elevations in blood leads which remained at acceptable levels of 0.4 ppm or less. Supplementation with 1 mg (a total of 1.3 mg lead in the diet) caused blood lead levels of 0.4 to 0.6 ppm. Blood leads of 0.4 to 0.6 ppm are considered suspicious of excessive lead exposures.

The acute toxicity of lead compounds varies considerably, ranging from 1.4 to 35,000 mg/kg depending on the species, route of administration, the compound and experimental conditions (7, 18). Lethal doses of lead acetate in the rabbit given intravenously ranged from 50 to 300 mg/kg and in the dog from 9 to 300 mg/kg for different investigators. This was also true for lead arsenate which ranged from 100 to 825 mg/kg administered orally to dogs. The individual values for these experiments are given below under Specific Paint Compounds.

Lead poisoning in human beings has been reported to have been caused by drinking of water containing lead in concentrations varying from 0.042 mg/l to 1.0 mg/l or more. However, concentrations of 0.01 to 0.16 mg/l have been apparently non-poisonous over long periods of time (13). For many years, the mandatory limit for lead in the USPHS drinking water standards was 0.1 mg/l; but in the 1962 Standards, the limit for lead was lowered to 0.05 mg/l. In the WHO International Standards and the WHO European Standards the limit for lead was set at 0.1 mg/l (13).

Specific Paint Compounds. There have been many studies on the toxicity of lead compounds. Tables 4 and 5 are taken from Spector (18) and Christensen (7) and are presented to emphasize the wide variation of responses of animals, discussed above, to the various compounds and methods of administration. An oral LD50 for rats for lead naphthenate (not in the tables) was found by Rochold (42) to be 3 gm/kg.

Three reports found in the literature involved the administration of lead in paint or paint materials to animals (53-55). White and Cotchin in 1948 (53) reported the results of a study of the absorption of lead paint, lead carbonate and lead acetate given to calves. The authors refer to a similar study by Haltenhoff who

Table 4. Toxicity data for lead compounds taken from Spector (18). References to the original literature are provided by Spector.

Compound	Animal	Route	Dose	Dosage mg/kg
				Value
	Rabbit	or	MLD*	400
	Rabbit	iv	MLD*	10
Lead	Rat	ip	LD	>1000[4]
	Guinea pig	ip	LD_{33}	100
	Guinea pig	ip	LD_{25}	200
	Pigeon	or	LD	160
Lead sulfate	Guinea pig	or	MLD*	35,000
	Guinea pig	ip	LD_{10}	146
	Guinea pig	ip	LD_{75}	290
	Dog	or	LD	2000-3000
Lead sulfide	Rat	ip	LD_{50}	1600
	Guinea pig	or	MLD	10,000
	Guinea pig	ip	LD_{50}	113
	Guinea pig	ip	LD_{33}	220
Lead tetraethyl	Rat	ip	MLD*	10
	Rabbit	oc	MLD	312-468
	Rabbit	iv	MLD	21.8-46.8
Lead acetate	Frog	oc	LD	1600
	Rat	ip	LD	130
	Rat	ip	LD_{50}	150
	Rabbit	oc	LD	300
	Rabbit	iv	LD	50
	Rabbit	iv	LD	300-400
	Cat	oc	LD	100
	Dog	or	LD	300
	Dog	oc	LD	80
	Dog	iv	LD	9
	Dog	iv	LD	300
Lead arsenate	Rat	or	LD_{50}*	825
	Rat	or	LD_{50}*	100
	Rabbit	or	LD_{50}*	125
	Rabbit	or	MLD	200
	Chicken	or	LD_{50}*	450
	Sheep	or	LD	4940[1]
Lead carbonate	Guinea pig	or	MLD*	1000
	Guinea pig	ip	LD	126
	Guinea pig	ip	LD_{75}	250
Lead chloride	Guinea pig	or	MLD	1500-2000
Lead chromate	Guinea pig	ip	LD_{75}	156
	Guinea pig	ip	LD_{66}	318
Lead diamide	Guinea pig	ip	LD_{33}	115
	Guinea pig	ip	LD_{66}	230
Lead lactate	Guinea pig	or	LD_{75}	1000-4000
Lead monoamide	Rat	ip	LD_{50}	400
	Guinea pig	ip	LD_{50}	100
	Guinea pig	ip	LD_{75}	210
Lead nitrate	Rat	ip	LD	270
	Guinea pig	or	LD	2000
Lead oleate	Guinea pig	or	LD	1000
Lead orthoarsenate	Guinea pig	ip	LD_{100}	140
	Guinea pig	ip	LD_{50}	38
Lead orthophosphate	Guinea pig	ip	LD_{33}	131
	Guinea pig	ip	LD	260
Lead oxide	Rat	ip	LD_{50}	450
	Guinea pig	or	MLD	2000
Lead (red)	Guinea pig	ip	LD_{66}	118
	Guinea pig	ip	LD_{50}	236
Lead silicate	Guinea pig	ip	LD	136
Lead stearate	Guinea pig	or	MLD	20,000

Table 5. Toxicity data for lead compounds taken from Christensen (7). References to the original literature are provided by Christensen.

Compound	Animal	Route	Dose	Dosage
Lead	Guinea Pig	ip	LDca	100
	Man	ih	LC	0.43mg/m^3
Lead Acetate	Rat	ip	LD50	150
		iv	LD50	120
Lead Arsenate	Rat	or	LD50	100
Lead Arsenate (basic)	Man	or	LDca	1.4
Lead Carbonate	Guinea Pig	ip	LDca	124
Lead Chloride	Guinea Pig	or	LDca	2000
Lead Chromate (vi)	Guinea Pig	ip	LD50	400
Lead Compounds-Triethyl-Chloride	Rat	ip	LD50	11
Lead Compounds-Triethyl-Oleate	Rat	or	LDca	50
Lead Dioxide	Guinea Pig	ip	LDca	115
Lead Fluoborate	Rat	or	LDca	50
Lead (11) Cyanide	Rat	ip	LDca	100
Lead (11) Fluosilicate	Rat	or	LDca	250
Lead Lactate	Guinea Pig	or	LDca	1000

Table 5. Continued

Lead Monoxide	Rat	ip	LD50	400
Lead Nitrate	Rat	ip	LDca	270
Lead Orthoarsenate	Guinea Pig	ip	LD50	38
Lead Orthophosphate	Guinea Pig	ip	LDca	131
Lead Oxide	Rat	ip	LD50	450
Lead Perchlorates	Mus	ip	LDca	275
Lead Silicate	Guinea Pig	ip	LDca	136
Lead Sulfate	Guinea Pig	ip	LD50	300
Lead Sulfide	Rat	ip	LD50	1600
Lead Tetbaethyl	Rat	or	LD50	35
Lead Tetrapropyl	Rat	ip	LD50	200
Lead Tetroxide	Guinea Pig	ip	LD50	220
Lead Titanates	Rat	ip	LD50	2000
Lead Triethyl	Rat	ip	LD50	11.2
Lead Trimethyl	Rat	ip	LD50	25
Lead Triphenyl Fluosilicate	Rat	or	LD50	100
Lead Tripropyl	Rat	ip	LDca	20

used red lead paint (lead oxide) with similar results. Calves were given single or repeated doses orally in gram quantities. The signs of poisoning and the concentrations of lead in the tissues were similar irrespective of the form of lead given. All animals died from their exposures. Nervous symptoms varied but included seizures, blindness and kidney degeneration. Flakes of lead paint could be detected in the stomachs days after administration. Concentrations of lead in the liver varied from 9.5 to 182 ppm and in the kidney from 0.5 to 300 pm.

Gage and Litchfield (54) studied the absorption of lead in rats given four polymer formulations in their diets: Polythene containing lead carbonate pearlescent pigment, polypropylene containing a lead chromate-molybdate pigment. PVC stabilized with tribasic lead sulphate and rigid urethane foam catalysed with lead 2-ethylhexoate. These polymers were fed at the level of 1% of the dietary formulations for 4 to 5 months. The lead contents of blood, bile, urine, liver, kidney and bone were measured. Control animals received no lead, and reference animals received 2, 6 and 20 ppm of lead as lead nitrate in their diet. Appreciable quantities of lead were absorbed from the PVC containing lead sulfate (containing 230 ppm as lead in the diet). The absorption of lead from the other

diets was not much different from that of the control diets. The authors concluded that lead was poorly absorbed from the rat intestine.

A second study by Gage and Litchfield (55) involved the absorption in rats of lead from paint films contained in the diet at a level of 1%. Two paint films were used: one containing middle orange chrome pigment and the other, lead naphthenate drier. The diets were fed up to 12 weeks. Control groups and reference groups using lead nitrate at 20, 50 and 100 ppm and lead napthenate at 100 ppm of the diet were also used. Blood, bone, kidney, liver, bile and urine lead determinations were made. The authors concluded that one-half of the lead in the chromate paint migrated (was absorbed) from the film under the experimental conditions.

Oral Hazard in Paints. The hazards of ingesting paint flakes containing lead has been the subject of considerable study. The above mentioned references (49-51) also provide review of this problem.

The Deputy Commissioner of Food and Drugs, James D. Grant, recently declared a limit of 0.06% of the total weight of the contained solids or dried paint film for paints to be used in or around the household (56). This decision was made on the bases of several publications,

announcements and testimonies (57-61). A detailed account of the bases for the Commissioner's decision is outside the scope of this survey. However, it perhaps should be pointed out that a daily permissible intake of lead for children (61) was based on the human lead balance studies of Kehoe (52), using a soluble lead compound, extrapolated to children and verified indirectly by studies on lead intoxicated children.

Lithium Compounds

Lithium Hydroxide	0 - 1%
Lithium Naphthenate	0 - 2%

Lithium is nonessential to man and is found in low levels in human tissues. The literature on the health effects of lithium compounds is relatively limited. Most of the information provided here comes from the "routine" references (4-26), especially Browning (6) and Stokinger (22). Schow, in 1957 (62), reviewed the pharmacology and biology of the lithium ion.

The body contains approximately 0.9 mg of lithium distributed throughout most of the tissues in levels of approximately 0.01 ppm. Being one of the alkali metals, Li behaves chemically in the body much like Na and K. Lithium compounds are moderately to highly toxic depending on the species, route of administration and the compound used. Sodium antagonizes the action of Li.

The most prominent symptoms of acute lithium poisoning in animals, when given by mouth or intravenously, include anorexia, nausea, vomiting, diarrhea, weight loss, dehydration and fall of body temperature. Effects on the central nervous system are manifested by muscular weakness, hyperirritability, stupor, and convulsion; on the heart by EKG changes, auricular standstill or fibrillation; on the kidney by oliguria, a rise in blood protein nitrogen and degenerative changes in the tubular epithelium. Many of these symptoms have been seen in humans in years past when lithium compounds were used therapeutically for gout, mental diseases and as a salt substitute.

Normal dietary levels of lithium were not readily available; however, lithium is readily absorbed from the gastrointestinal tract (greater than 70%) and excreted in the urine (31). Lethal oral doses of lithium compounds range from 0.025 to 200 mg/kg. Information on chronic oral exposures is lacking; however, the industrial TLV (4) for the highly toxic lithium hydride is set at 0.025 mg/cu. m. because it is intensely irritating and corrosive. No limits have been set for drinking water; however, Hibbard recommends, without references, that lithium should not exceed 5 mg/l (13).

Specific Paint Compounds. The hydroxide is is strongly alkaline and caustic in high concentrations. Information on the naphthenate was not readily available.

Oral Hazard in Paint. Because of the highly toxic nature of lithium compounds, studies should be carried out to confirm the safety of any levels of those materials in paints.

Magnesium Compounds

Magnesium Aluminum Silicate	0 - 20%
Magnesium Oxide	0 - 1%
Magnesium Silicate	0 - 50%

Magnesium is abundantly distributed in nature and is an essential element. There is a large literature on the biological role of Mg in living systems. Schroeder et al. (69), Browning (6) and Stokinger (22) provide recent views of the essentiality and toxicity of magnesium compounds.

Magnesium is the second most abundant divalent cation in the body amounting to a total of about 35 gm, 70% of which is found in bone (980 ppm). Cartilage contains 200-300 ppm while other tissues contain from 100 to 200 ppm (12). On normal diets containing 180 and 360 mg/day (24), one-third of the dietary intake appeared in the urine, the other two-thirds appearing in the feces. Aside from its structural functions in bone and teeth, magnesium is important in neuromuscular conduction of skeletal and cardiac muscle and to the activity of numerous enzymes involved with oxidative-phosphorylation, protein, lipid and carbohydrate metabolism. Magnesium deficiency produces symptoms of hyperirritability (tetany) sometimes

seen in patients on i.v. fluid therapy inadequate in magnesium. In cattle, magnesium deficiency produces "grass staggers".

Magnesium compound toxicity varies from slightly to highly toxic depending on the species, route of administration, and the compound used (7, 18). When administered intravenously, magnesium salts can produce general anesthesia, narcosis and muscular paralysis which can be counteracted by intravenous calcium administration. Industrial TLV (4) for magnesium is set at 10 mg/cu. m. for MgO fumes because of fume fever reactions.

Oral ingestion of magnesium is considered relatively non-toxic to man. Magnesium acetate, however, has an oral LD50 of 18 mg/kg (highly toxic) in the mouse. At high concentrations, magnesium salts have a laxative effect. Drinking water standards do not impose maximum allowable concentrations but do suggest limits under 150 mg/l primarily for taste problems.

Specific Paint Compounds. Magnesium Oxide is used as a dietary supplement for magnesium and therapeutically as an antiacid and cathartic and can be given in gram quantities safely. Long-term use of Mg compounds as laxatives can develop dependency (constipation) as the only apparent adverse effect from their use (6). Magnesium silicate (talc) has been "generally recognized as safe" (FDA's GRAS list) as an anticaking agent in table

salt up to 2% and in vanilla powder and in vanilla-vanillin powder under food standards (29). Information on magnesium aluminum silicate was not readily found but this compound might be expected to behave similarly to magnesium silicate.

Oral Hazard in Paints. Because of the low acute or chronic oral toxicity of magnesium compounds, the oral hazard due to magnesium in paints is probably quite low.

Manganese Compounds

Manganese Dioxide	0 - 2%
Manganese Naphthenate	0 - 1%
Manganese Soaps	0 - 1%

Manganese is widely distributed in nature and is an essential element for both plants and animals. There is a relatively large literature dealing with normal, deficiency and toxic states of manganese. Cotzias (56), Schroeder (67), Browning (6), Stokinger (22), and Smith (48) provide recent reviews of manganese health literature.

Manganese is involved with the functions of numerous enzymes governing carbohydrate, lipid, protein metabolism and oxidative phosphorylation, including arginase, alkaline phosphatase, prolidase, carboxylase, cysteine desulfhydrase, thiaminase, deoxyribonuclease, glycyl-l-leucine dipeptidase and other enzymes (67).

Parenterally administered lethal doses of manganese compounds vary from 0.12 to 410 mg/kg (7, 18) depending on the species, route of administration and the compound. Organic manganese compounds tend to be considerably more toxic than inorganic compounds. In chronic exposures of human beings, manganese is a nerve toxin, with polymorphic manifestations of psychic and neurological disorders. Manganese can also cause a pneumonia-like condition known as "manganese pneumonitis" (6). Acute exposure to manganese fumes can cause metal fume fever. The industrial TLV for manganese is set at 5 mg/cu m. (4).

The body contains about 20 mg of manganese with most of the tissues containing 0.1 to 0.2 ppm (12). The kidney, liver, and pancreas contain 0.18, 1.3 and 1.16 ppm, respectively. Tipton and Stewart's (24) subjects over a 347 day period averaged 3.3 and 5.5 mg/day in the diet, 2.5 and 3.0 mg in the feces, and 0.04 and 0.05 mg of manganese in the urine.

Manganese is considered only slightly toxic orally. The oral LD50 of manganese acetate for the rat was 3.7 gm/kg (7) while daily oral doses of 0.5 to 6.0 gm/kg in the rabbit produced decreased growth and bone development (13). A small outbreak of an encephalitis-like disease, with early symptoms of lethargy and edema, was traced to manganese in the drinking water in a village outside of Tokyo; three persons died as a result of poisoning by well water contaminated by manganese derived from dry-cell batteries buried nearby (13). There are no limits set on the amounts of manganese in domestic water supplies.

The normal dietary intake is far higher than the amount that would be tolerated esthetically in drinking water (13).

Specific Paint Compounds. No toxicological information on the specific compounds of interest was readily available.

Oral Hazard in Paints. Because manganese compounds are poorly absorbed and the amounts of such compounds used in paints are relatively small (2% or less), their use in paint probably provides low toxic hazard.

Mercury Compounds

Phenyl Mercuric Acetate	0 - 0.5%
Mercury Cadmium Lithopone	0 - 15%
Phenyl Mercuric Oleate	0 - 0.5%
Mercury Soaps, other	0 - 0.5%

Mercury is a nonessential element for humans and its toxicological history dates back to the earliest of medical writers. There is an extensive health literature on mercury which recently has grown at an explosive rate in response to the concerns of mercury contamination in the environment. Bidstrup (69), Stahl (70), Friberg et al. (71), Friberg et al. (72) and Goldwater and Clarkson (73) represent just a few of the recent reviews on mercury toxicity.

Mercury is considered highly toxic to man. The

signs and symptoms are numerous and depend on the compound and the rate and the route of exposure. Acute severe exposures may produce abdominal pain, vomiting, diarrhea, gingivitis, pneumonitis, renal damage, circulatory failure, and respiratory failure. Chronic excessive exposures may result in one or more of the three classical signs of gingivitis, tremor and emotional instability (10). Lethal doses in animals range from 16 to 500 mg/kg. Three to thirty gm of mercury have been fatal to man. The industrial TLV for alkyl mercurial compounds is 0.01 mg/cu. m. and for other mercury compounds, 0.05 mg/cu. m. (4).

The diet normally contains about 5 micrograms daily of mercury, most of which is absorbed and excreted in the urine (26). The drinking water standards of the USPHS and the WHO do not include limits for mercury but the maximum permissible concentration of mercury or mercuric ions in drinking water in the USSR has been set at 0.005 mg/l. According to one investigator, adults may safely drink water containing about 4-12 mg of mercury (inorganic) per day and a fatal dose of such water would be 75 to 300 mg/day (13).

Specific Paint Compounds. Oral LD50s for phenyl mercuric acetate were reported as 40 mg/kg for the rat and 70 mg/kg for the mouse. Quantitative toxicity data on the other mercury compounds were not readily found.

Oral Hazard in Paints. The amount of mercury to be used in paints is relatively small. However, due to the highly toxic nature of mercury compounds, the possibility of chronic exposures (months), and the possible increased susceptibility of young children, studies should be made to ensure safe levels of mercury used in paints.

Molybdenum Compounds

Lead Molybdate	0 - 15%
Zinc Molybdate	0 - 25%

Molybdenum is essential for certain plants and animals. Toxicity data on humans is limited. Fairhall (75) provides a summary of industrial exposures. More recent reviews include those of Browning (6) and Stokinger (22).

Molybdenum compounds are moderately toxic in animals. Lethal doses for molybdenum compounds in animals ranged from 100 to 500 mg/kg (7, 18, 22). Available information concerning exposure to molybdenum compounds in industry is insufficient to define a health hazard (10); however, based on animal studies, the TLVs are set at 5 mg/cu. m. for soluble molybdenum compounds and 10 mg/cu. m. for insoluble compounds (4).

The body contains an estimated 5 mg of Mo with most of the tissues containing 0.1 ppm or less. Bone, liver, adrenal and kidney contain 1.5, 1.1, 0.6 and 0.4 ppm, respectively (12). The diets reported by Tipton and Stewart (24), contained 0.21 and .46 mg/day half of which was ex-

creted in the feces and half in the urine.

There are no limits set on the amount of molybdenum in drinking water; however, molybdenum levels in feeds and domestic animals have been of concern (13). Five mg/day given to rats in their water caused increased mortality (13).

Specific Paint Compounds. No quantitative toxicity data on these compounds were readily found.

Oral Hazard in Paints. Insufficient information is available to estimate oral hazards for humans. Adequate studies will need to be performed to establish safe levels of these molybdenum compounds in paints.

Nickel Compounds

Cobalt Nickel Titanate	0 - 20%
Nickel Antimony Titanate	0 - 15%
Nickel Titanate	0 - 15%

There is a considerable literature on the health effects of nickel. Recent reviews include those of Sullivan (76), Schroeder (77) and Smith (48), as well as Browning (6) and Stokinger (22). Nickel is considered nonessential to man. Most of its toxicological concerns in man have centered on the industrial use of nickel carbonyl. The TLV for nickel carbonyl is 0.007 mg/cu. m., for other nickel compounds, 1.0 mg/cu. m. Nickel carbonyl

has been associated with an increased incidence of cancer of the lung and ethmoid sinuses in men exposed to dust in nickel refining.

Nickel salts are considered to be highly toxic following access to the blood stream (22). Acute lethal doses in animals range from 5 to 1620 mg/kg (7, 18). Systemic poisoning by nickel salts in humans, however, is unknown (6). Allergic contact dermatitis is not infrequent with skin exposures.

The body contains about 10 mg of nickel with most tissues containing approximately 0.1 ppm (12). Bone, skin, tongue, lung and adrenal contain 2.0, 0.44, 0.24, 0.27, and 0.28 ppm, respectively. The diet contains about 450 micrograms of nickel per day. In Tipton and Stewart's study (24), the diets contained 0.39 and 0.81 mg, the feces 0.22 and 0.35 mg and the urine 0.11 mg each.

Orally, chronic administration of 2 mg of nickel per day in the drinking water of rats caused no harm; however, 10 to 20 mg/kg proved fatal to dogs (13). The USPHS Drinking Water Standards do not place a limit on nickel; however, it is reported that in Russia, the maximum permissible concentration is 1.0 mg/l (13).

Specific Paint Compounds. Quantitative toxicological data for these compounds were not readily found in the literature.

Oral Hazard in Paint. Nickel and titanium (see Titanium Compounds, below) compounds tend to have low toxicity with oral administration and probably offer low hazard risks in paints at the levels used. Antimony and cobalt (see individual sections above) offer considerable potential hazard and these compounds should be evaluated experimentally to determine safe levels for paints.

Strontium Compounds

Strontium Chromate	0 - 25%

Except for radioactive strontium, strontium compounds are considered relatively non-toxic to man, similar to calcium compounds (6, 10, 16, and 22). Since chromates are toxic, strontium chromate is discussed under Chromium Compounds, above

Tin Compounds Organic (specific compounds)

Tributyl Tin Oxide	0 - 1%
Tin Organo Compounds	0 - 1%

The full toxicity of tin is observed almost exclusively from its organic compounds - the alkyl derivatives (5). Tin itself when taken by mouth is practically innocuous, but its dust or fume when inhaled can cause a benign, symptomless pneumoconiosis. The TLV for inorganic tin (except tin hydride and tin oxide) is 2 mg/cu. m. (4). The alkyl derivatives are highly toxic and one of them,

diethyl tin, has proved lethal to human beings with symptoms of cerebral edema and gastrointestinal disturbance (6). Certain organo tin compounds, especially the tri-butyl series, are potent skin irritants. The TLV for organic tin compounds is 0.1 mg/cu. m. (4).

Numerous articles on the toxicity of tributyl tin oxide and other alkyl tin compounds (78-81) and other organo tin compounds are available in the Kettering Library. Elsea and Paynter (78) found the acute oral LD50 for tributyl tin oxide to be 148 mg/kg (moderately toxic) for rats. The oxide fed to rats in the diet at levels of 32, 100 and 320 ppm suppressed growth. Stoner et al. (79) and Barnes and Stoner (80) studied a series of tetra-, tri-, di- and mono-alkyl tin compounds in rats, rabbits, guinea pigs, and fowls in both acute and chronic experiments. In rabbits, triethyl tin, the most active compound, produced muscular weakness, tremors and death. Other species and compounds showed variations of this pattern. The outstanding sign of chronic poisoning was muscular weakness.

Oral Hazard in Paint. Since organo tin compounds are moderately to highly toxic in animals and man, the use of these compounds in paints should be adequately studied to determine the levels which can be used safely.

Titanium Compounds

Titanium Dioxide	0 - 50%
Titanates:	
Antimony	0 - 15%
Nickel	0 - 15%
Tungsten	0 - 15%
Cobalt Nickel	0 - 20%

Titanium is widely distributed in the earth's crust where it is the eighth element in abundance. It is not essential for plants or animals nor is it regarded as toxic to animals or humans. The lack of toxicity of titanium and its compounds by contact with skin and tissues has been amply demonstrated by its use in the therapy of skin disorders and as a surgical prosthesis (6).

The body contains an estimated 15 mg of titanium with most of the tissues containing approximately 0.1 ppm or less. Lung contains about 2.8 ppm and the bone 1, the thyroid 0.49 and the skin 0.61 ppm. Titanium accumulates in the lung with age, apparently due to polluted air. Tipton and Stewart's studies (24) indicated 0.75 and 2.0 mg/day in the normal diet with 0.46 and 0.82 mg/day and 0.49 and 0.47 mg/day appearing in the feces and urine, respectively. Oral administration of large amounts of titanium salts mixed with the diet is stated by Ereaux not only to have no toxic effect but actually to have an improvement on health (6). There are no water drinking limits set for titanium (13).

Specific Paint Compounds. Antimony, cobalt, nickel, and tungsten are discussed in other sections of this survey. Titanium dioxide is used as a food additive (29) and is considered to be chemically inert in the body (82, 83, 4, 6, 22). The TLV for titanium dioxide is set at 10 mg/cu. m.

Oral Hazard in Paint. Antimony, cobalt, nickel and tungsten possess significant toxicities of their own and should be considered on individual bases (see corresponding sections in this survey for these metals). Titanium dioxide is apparently inert and should pose no oral hazard in paint formulations.

Tungsten Compounds

Tungsten Titanate 0 - 15%

The literature on the health effects of tungsten is limited. Stokinger (22) and Browning (6) provide recent reviews on tungsten; however, the literature cited is not very recent.

Tungsten is nonessential to humans. Data on the body burden (12), dietary levels (26, 24) or on the absorption of tungsten (31) were not readily found.

Data on the toxicity of tungsten compounds was also limited (7, 18). The following, taken from the "Documentation of Threshold Limit Values" (4), represents

similar data presented in Browning and Stokinger. The LD50 of sodium tungstate was between 140 to 160 mg/kg when injected subcutaneously into adult rats, making this compound moderately toxic. On oral administration to rats, the toxicity of this compound was greater than that of tungsten oxide while ammonium paratungstate was the least toxic of the three. Both sodium tungstate and the oxide proved lethal to rats on a diet containing 0.5% as W. The ammonium salt was not lethal at this level but resulted in weight loss (4-50%). A similar weight loss was produced by dietary levels of 0.1% of the oxide and the sodium salt. Tungsten powder when fed to weanling rats of both sexes at levels of 2, 5 and 10% of the diet resulted in a 15% reduction in body weight gain among the females but not the males.

Long industrial experience has indicated no pneumoconiosis among workers exposed solely to W or its insoluble compounds. Dust chamber exposures of animals to W, tungsten dioxide and tungsten carbide produced only minor pulmonary changes. The TLV for soluble tungsten compounds is 1 mg/cu. m. and for insoluble compounds, 5 mg/cu. m.

Calcium, magnesium and iron salts of tungsten are insoluble; hence they are not likely to occur in natural waters or to remain in solution in waste waters

from industry. Therefore, there are no limits set for tungsten in domestic water supplies (13).

Specific Paint Compounds. Toxicological data on tungsten titanate was not readily found.

Oral Hazard in Paint. Since tungsten compounds can be significantly toxic, adequate investigation should be made to establish the safety of using tungsten titanate in paint at the 15% level used in paints.

Zinc

Zinc Chromate	0 - 25%
Lithopone	0 - 50%
Zinc Metal	0 - 80%
Zinc Molybdate	0 - 20%
Zinc Napthenate	0 - 1%
Zinc Oxide	0 - 25%
Zinc Soaps (other than stearate)	0 - 1%
Zinc Stearate	0 - 5%
Zinc Sulfide (in Lithopone)	0 - 15%

Zinc is widely distributed in nature and is an essential element to humans. There is a large literature on the biological importance of zinc, primarily dealing with zinc deficiency, metabolism and its role in metalloenzymes and less so on the toxic effects of zinc compounds.

Browning (6) and Stokinger (22) provide recent reviews of the literature on zinc toxicity.

Zinc salts in high enough concentration are astringent and corrosive to the skin and irritating to the gastrointestinal tract (22). When ingested they act as emetics. Zn ion, however, is ordinarily too poorly absorbed to induce acute systemic intoxication. After large doses have been ingested, fatal collapse may occur as a result of serious damage to the buccal and enteric mucous membranes.

In industrial exposures, zinc chloride fumes have been found to cause damage to the mucous membranes of the nasopharynx and respiratory tract. The TLV of the chloride fume is set at 1 mg/cu. m. The TLV for zinc oxide is set at 5 mg/cu. m. due to its ability to induce metal fume fever (zinc chills, brass founder's augue, etc.).

The human body content of Zn is estimated to be about 230 mg. Most of the tissues contain from 3 to 30 ppm with high concentrations being found in bone, kidney, liver, muscle and prostate (12). Tipton and Stewart (24) found normal diets to average 11 and 18 mg/day with most of this excreted in the feces (14 and 16 mg/day) and about 10% excreted in the urine (1.3 and 1.2 mg/day).

Acute oral lethal doses for Zn compounds listed in Spector (18) and Christensen (7) range from 40.5 to 2460 mg/kg depending on the species and compound. There

have been numerous cases of food poisoning from the use of galvanized containers. Six hundred and seventy-five to 2280 mg/l has been reported to have an emetic effect. Ingestion of 6 gm of zinc chloride has been fatal in man.

The USPHS 1962 limit for zinc in drinking water is set at 5 mg/l based on the bad taste (13). Community water supplies have been reported with 11.2, 17, 18.5 and 25.6 mg Zn/l with no ill effects. Pigs drinking water containing 1000 mg/l developed lameness and malnutrition. Rats, however, receiving 1000 mg/l showed no effect. In these latter studies, rats receiving 5000 mg Zn/l had slight toxic effects and rats receiving 10,000 mg/l experiences decreased growth rates and early death.

Specific Paint Compounds. Lithopone, liberates hydrogen sulfide upon decomposition by moisture or acids (14, 16). Zinc oxide is used as a trace mineral food supplement (29) and in skin ointments. It is considered relatively non-toxic orally. Freshly formed ZnO fumes can be toxic to workers in industry (4). Zinc Naphthenate was reported by Rockhold (42) to have an oral LD50 greater than 6 gm/kg in rats, which makes it of low acute toxicity for rats. Zinc stearate, like zinc oxide, is used as a dietary and nutritional supplement but is toxic, producing pulmonary fibrosis, when inhaled. Zinc metal is considered by Sax (16) as not inherently toxic.

Oral Hazard in Paint. Most of the zinc compounds of interest do not appear to offer much of an oral hazard at the concentrations used in paints. Some of these compounds such as the chromate and possibly the molybdate, may be toxic because of the accompanying anion and therefore should be adequately evaluated to determine safe levels. Although zinc metal is relatively inert biologically, the use of it at an 80% level in paint may lead to the formation of the zinc chloride in the stomach which could produce toxic effects.

Zirconium Compounds

Zirconium Naphthenate	0 - 2%
Zirconium Oxide	0 - 1%
Zirconium Soaps	0 - 2%

Zirconium is not essential to man. Browning (6), Stokinger (22) and Schroeder and Balassa (84) provide recent reviews of zirconium toxicity.

Zirconium is relatively non-toxic to animals and there is no well authenticated evidence of toxic effects from industrial exposure (6). However, there have been reports of pulmonary granulomas in zirconium workers and granulomatous skin lesions from its use in deodorant sticks (16). The TLV for zirconium compounds is 5 mg/cu. m. (4).

The body contains about 6 mg of zirconium. In Tipton and Stewart's (24) study, normal diets contained 0.43 and 0.55 mg/day with 0.12 and 0.059 mg appearing in the feces and 0.08 and 0.18 mg appearing in the urine, providing for an average positive balance of 0.23 and 0.31 mg/day over the 347 day period. Retained zirconium is thought to accumulate in bone (6).

There are no limits for zirconium in drinking water (13). The toxicity of Zr salts is very low by the oral route; the LD50 dose of the nitrate, chloride, sulfate, and acetate of Zr and sodium zirconyl sulfate for rats ranged from 2.5 to 10 g/kg (22). Intraperitoneally, the same Zr compounds were considerably more toxic acutely, (LD50's from 0.175 to 4.1 g/kg). Hydrated Zr carbonate is physically inert in rats in oral doses up to 10 g/kg. Zr gluconate, however, was moderately toxic (LD50, 247 mg of ZR/kg) acutely by intraperitoneal administration in rats.

Animal studies reported by Rothstein (in 13) indicated neither acute or chronic injury in response to Zr compounds given orally for as long as two years. Even 20% Zr oxide in the diet was not harmful.

Specific Paint Compounds. Zirconium oxide is relatively non-toxic orally. Toxicological data on the other Zr compounds was not readily found.

Oral Hazard in Paint. Zirconium compounds have low toxicity orally and probably represent little oral hazard when used in paints at levels of up to 2%.

IV. Summary

This study was intended to provide a preliminary survey of the literature pertaining to the potential hazards of ingesting paints containing metals. Over 100 specific compounds containing 25 different elements were reviewed for possible inclusion in this report.

As was expected, very little experimental data were available on the ingestion of paints containing metals, e.g., only three articles were found on leaded paints. Relative to the toxicity of specific compounds per se, again there were few data which could be used to predict ingestion hazards for acute or chronic exposures in children or adults.

Each section on the different compounds in part III contains a summary of hazards for that elemental class. As an overall summary, aluminum, calcium, magnesium, manganese, strontium, titanium and zirconium compounds are generally of low oral toxicity. Except when toxic components (such as antimony in antimony titanate) are contained in the formulation, these compounds should be of low oral hazard.

Compounds of antimony, barium, cadmium, lead, lithium, and mercury are generally highly toxic and should be limited to low levels in paints. Compounds of boron, cobalt, chromium, copper, molybdenum, tungsten and zinc vary from slightly to highly toxic depending on the chemical form and therefore need to be evaluated on individual bases.

Table 6 presents a listing of most of the specific compounds, their ranges of concentrations used in paints, and crude estimates of oral hazards in paints based on the findings of this survey.

The concern of the paint industry for potential hazards of the ingestion of paints involves both acute and chronic exposures of children to specific paint formulations. Most of the known toxicity of the compounds considered in this report is based on animal experiments (acute and chronic) and on human experiences (mostly acute intoxication) of exposures to compounds which might not be related closely enough chemically to the compounds of interest. Therefore, any conclusions based on this study should be adequately verified by animal and human experiments with flakes from commercially formulated and applied paints (see recommendations below).

Table 6. Preliminary Estimates of Oral Hazard for Specific Compounds in Paints.

Table Legend: The ranges indicate the percentages of the compounds (~~based on dry film~~) ~~used in paints~~. The predicted oral hazards are only crude estimates based on toxicity data derived from this search of the literature. Hazard ratings are 0, 1, 2 and 3 for no, slight, moderate and high relative hazard, respectively. A dash in the hazard column indicates insufficient data available to make an estimate. An asterisk indicates that the estimate is based loosely on information about the general class of the compound. Note: Many compounds have several oxides depending on the valence states. The designation of "soap" refers to salts of oleic, lauric, palmitic, stearic and erucic acids.

Compound	Range (%)	Oral Hazard
Aluminum Hydroxide	0 - 5	0
Aluminum Metal	0 - 5	0
Aluminum Oxide	0 - 5	0
Aluminum Silicate	0 - 5	0*
Aluminum Stearate	0 - 10	0*
Antimony Oxide	0 - 10	0 - 1
Barium Meta Borate	0 - 15	2*
Barium Soaps	0 - 3	2*
Barium Sulfate	0 - 30	0
Barium Sulfide (Lithopone)	0 - 50	0 - 1
Boron Trifluoride	0 - 1	2 - 3
Cadmium Barium Soaps	0 - 3	3*
Cadmium Lithopone	0 - 15	3*
Cadmium Selenide	0 - 15	1*
Cadmium Selenide Pigments	0 - 25	1*
Cadmium Soaps	0 - 3	2 - 3*
Cadmium Stearate	0 - 3	2 - 3*
Calcium Carbonate	0 - 70	0
Calcium Naphthenates	0 - 2	0
Calcium Oxide	0 - 15	0

Table 6. Continued

Calcium Soaps	0 - 2	0
Chromium Oxide	0 - 15	1 - 3
Cobalt Naphthenate	0 - 1	0 - 1
Cobalt Nickel Titanate	0 - 20	2*
Cobalt Soaps	0 - 1	2*
Copper Metal	0 - 1	2*
Copper Naphthenate	0 - 5	0 - 1
Copper Oxide	0 - 25	2*
Copper Phthalocyanine	0 - 5	-
Copper Soaps	0 - 1	0 - 1
Lead Carbonate Basic	0 - 60	3*
Lead Chromates	0 - 25	3*
~~Lead Chromates VI~~	0 - 25	3*
Lead Metal	0 - 25	3*
Lead Molybdate	0 - 15	3*
Lead Naphthenate	0 - 3	3*
Lead Oxides	0 - 50	3*
Lead Silicate Basic	0 - 15	3*
Lead Silico-Chromates	0 - 25	3*
Lead Soaps	0 - 3	3*
Lithopone	0 - 50	0 - 1
Lithium Hydroxide	0 - 1	2 - 3*
Lithium Naphthenate	0 - 2	2 - 3*
Magnesium Aluminum Silicate	0 - 20	0*
Magnesium Oxides	0 - 1	0
Magnesium Silicate	0 - 50	0
Manganese Dioxide	0 - 2	1 - 2
Manganese Naphthenate	0 - 2	0 - 1
Manganese Soaps	0 - 1	1 - 2
Mercury Soaps	0 - 0.5	2 - 3
Nickel Antimony Titanate	0 - 15	2*
Nickel Titanate	0 - 15	2*
Phenyl Mercuric Acetate	0 - 0.5	3*
Phenyl Mercuric Oleate	0 - 0.5	3*

Table 6. Continued

Sodium Tetraborate	0 - 15	2*
Strontium Chromate	0 - 25	-
Titanium Dioxide (commercial grades)	0 - 50	0 - 1
Tributyl Tin Oxide	0 - [illegible]	3*
Tin Organo-Compounds	0 - [illegible]	3*
Tungsten Titanates	0 - 15	2*
Zinc Chromates	0 - 25	-
Zinc Metal	0 - 80	2*
Zinc Molybdate	0 - 20	2*
Zinc Naphthenate	0 - 1	0 - 1
Zinc Oxide	0 - 25	0 - 1
Zinc Soaps	0 - 1	0 - 1
Zinc Stearate	0 - 5	0 - 1
Zinc Sulfide (Lithopone)	0 - 50	0 - 1
Zirconium Naphthenate	0 - 2	0
Zirconium Oxide	0 - 1	0
Zirconium Soaps	0 - 2	0

V. Recommendations

Recommendation 1.

The purpose of this survey was to examine superficially the literature on the potential hazards of ingesting paints containing metallic constituents. The survey did not yield much information on which to base standards for permissible levels of metals in paints. In this author's view, an exhaustive literature search on each of the specific compounds or elemental classes of compounds would not be especially productive either. However, before undertaking laboratory experiments to generate the required data, more detailed, but not exhaustive, literature searching should be carried out in order to give direction to the initial experiments. Automated literature searching techniques such as those provided by Medlars or Medline of the National Library of Medicine or by Chemical Abstracts could be used. Utilizing the additional literature contained in the Kettering Library files would also provide considerably deeper coverage.

Recommendation 2.

Man is his own best model and any conclusions based on animal data should be, if at all possible, confirmed by human studies such as those cited for lead. Before human studies are undertaken, extensive studies using animals will need to be conducted in order to

characterize the degree of toxic hazard, both acute and chronic; to determine the mechanisms of toxicity and early indicators of toxic effects; and to determine the degree of absorption, the distribution patterns and the rates of excretion. Only when safety seems assured should small quantities of the paint flake materials be given to children or adults to make certain that the types of metabolism and the degree of absorption are similar to test animals.

It is beyond the scope of this study to detail the types of experiments which should be carried out. However, in addition to the studies involving the health hazards of lead exposures (49-61), the reader is referred to such documents as those of Lehman (85), Fitzhugh (86), Irwin (87), and the National Academy of Science (88) for background in toxicological testing.

Recommendation 3.

Studies used for predicting the hazards due to metal-containing paints should involve the use of the metal-containing paint formulations themselves. Toxicological information on pure compounds or related metal compounds should not be considered a sufficient substitute for actual paint flake ingestion studies. Paint fillers, binders, modifiers, etc., may increase the absorption of the metals concerned, or as is most likely, they may reduce the toxic hazards by reducing the solubility of the metals in intestinal juices.

Recommendation 4.

Since there is a large number of compounds and varieties of paint formulations, it is desirable to develop *in vitro* testing techniques for screening purposes. Crampton (89) and others describe a number of *in vitro* methods such as closed loops, inverted sacs, etc., which could be used. Solubility studies using synthetic intestinal juices have been discussed with members of the National Paint and Coatings Association on previous occasions. Any *in vitro* studies should be validated for their ability to predict *in vivo* behavior.

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