44460

March 12, 1991
Project No: 400754

March 12, 1991

Mr. Randy Sturgeon
Enforcement Project Manager
U.S. Environmental Protection Agency
Region III
841 Chestnut Street
Philadelphia, Pennsylvania 19107

Dear Mr. Sturgeon:

SUBJECT: Du Pont Newport Site, Newport, Delaware
Supplemental Phase III RI Tasks

Introduction

This letter serves as a response to the EPA's August 9, 1990, letter and the EPA's subsequent request of January 8, 1991, to address the need for further evaluation of the pigment-colored sediments observed at the northern riverbank along a portion of the Ciba-Geigy Newport Plant area and concerns for off-site historical are emissions. Furthermore, this letter is submitted in lieu of a Final Work Plan-Volume II, which is no longer deemed necessary for this project.

As agreed to during Du Pont's and the EPA 's January 8, 1991, meeting, Du Pont has conducted a comprehensive literature search regarding the toxicity of the pigments associated with the historical operations at the Newport Site. In addition, Du Pont and Woodward-Clyde Consultants (WCC) have reviewed the historical aerial photographs of the city of Newport to evaluate the feasibility of off-site soil sampling. Each of these areas of concern are addressed separately below.

Pigment Colored Riverbank Sediments

Our review of the history of the riverbank operations suggests that during the 1950's, pigment products awaiting transport were stored in drums on pallets over gravel along the riverbank. This form of outdoor storage was conducted in accordance with standard practices of the time and is still an acceptable industry practice today. Occasional loss of drum integrity resulted in some accidental release of pigment product to the underlying soils along the riverbank.

The transport mechanisms by which pigment migrated from the underlying soils to the riverbank sediments is not clearly defined. However, it can be deduced from the pigments' physical and chemical properties, and riverbank hydraulics, that the transport mechanism primarily involved the movement of pigments with colloidal particles or suspended solids in groundwater due to preferential sorption. The rationale for this deduction is based on the high molecular weight and low water solubility of the copper phthalocyanine (CPC), Quinocridone (QA), Lithopone, and titanium dioxide (Ti).

The observed pigment-colored sediments along the riverbank do not appear subject to erosion by the river because they occur in an area of fine-grained sediment deposition. The limited quantity of pigment-colored sediment over a small geographical area also suggests a very slow pigment deposition mechanism. The stability of the pigments, as documented in the appended

literature, is supported by the presence of the pigments in the riverbank sediments. Most of these pigments were released to the riverbank decades ago. If these pigments were water soluble or subject to even very slow degradation processes, the sediments would not carry their colors today. Thus, the toxicity data of the original pigments is relevant to the evaluation of the potential impact to the environment associated with pigment-colored sediments currently present along the riverbank.

Available literature data for the pigments produced at the site are presented in the appendices listed below. The literature reference for lithopone refers to the components of the pigment, i.e., zinc sulfide, barium sulfate and some zinc oxide, therefore, these components are provided independently.

Appendix A CPC
Appendix B QA
Appendix C Barium
Appendix D Barium Sulfate
Appendix E Zinc
Appendix F Zinc Oxide
Appendix G Zinc Sulfide
Appendix H Titanium Dioxide

Solubility of Pigments

Physical and chemical properties of the pigments previously and currently produced at the Newport Site are provided in Appendices A through H. These pigments are all considered insoluble in water. QA is also found to be insoluble in many classes of organics. Barium sulfate is slightly soluble in strong acids, which are found in groundwater conditions.

Toxicity of Pigments

Appendices A through H provide comprehensive toxicity literature for the pigments, along with the corresponding references. A summary of toxicity data for individual pigments and pigment-related compounds is provided below:

CPC: A very low acute oral toxicity is attributed to CPC, with no deaths or clinical signs of toxicity in rats administered up to 17 grams/kg. Rat testing indicates that CPC is a mild skin irritant. No carcinogenic or embryotoxic data is available; however, CPC was not mutagenic in the Ames bioassay.

QA: Acute toxicity data for QA indicate mild skin irritation effects to animals and demonstrates a high lethal dose 50 (LD_{50}) of greater that 11,000 mg/kg. Carcinogenic data available indicates that QA is non-carcinogenic.

Barium Sulfate: The barium sulfate literature indicates that the acute toxicity is low with no documented animal or human deaths at reasonably high doses. During carcinogenic studies, no tumors were reported in three generations of feeding mice and monkeys. Barium sulfate was also found to be non-toxic to fish in concentrations up to 100,000 parts per million (ppm).

Zinc Oxide: Besides barium sulfate and zinc sulfide, low levels of zinc oxide is also associated with the production of Lithopone. Zinc oxide is commonly used as a topical dermatological preparation and has demonstrated some instances of skin irritation in humans. Toxicity of ingested zinc compounds, including zinc oxide is low. Long-term occupational exposure to high levels of zinc dust has shown gastro-intestinal irritation. Since zinc is a necessary component of human metabolism, its toxicity potential is extremely low and only occurs under heavy occupational exposures to zinc oxide powder. Since the zinc oxide is structurally bound in Lithopone, it does not exist as a powder at troublesome concentrations. Therefore, risk to human health and the environment is highly unlikely as a consequence of its presence in the riverbank sediments.

Zinc Sulfide: This associated component of the Lithopone process is extremely insoluble in water with a solubility of 0.00069 grams/100 cc at 18°C. As previously stated, zinc salts including zinc sulfide are relatively nontoxic to humans (and all other mammals) due to efficient zinc homeostatic mechanisms. Effects of ingestion and exposure to zinc sulfide are synonymous to those of zinc oxide. Therefore, the risk to human health and the environment from zinc sulfide at the present concentrations and physical form are considered negligible.

Titanium Dioxide: This white pigment is used in a variety of applications from polymer coatings to the food industry. It is insoluble in water and only soluble in hot sulfuric acid and extremely strong alkalies. Ti has very low acute toxicity in mammals and has not been found to be carcinogenic. Aquatic environmental studies indicate that Ti has low toxicity. These environmental studies also indicate that lethal and sublethal measured effects during exposure to Ti manufacturing effluents to aquatic fauna were more likely due to changes in water chemistry from the effluent (pH, oxygen, etc.) than actual toxicity due to Ti. Dilution of the effluents resulted in no lethal observations. Therefore, low concentrations of Ti that may be present in pigment-colored sediments do not appear to pose a risk to human health or the environment.

Barium Sulfate, Titanium Dioxide and CPC have been approved for use as pigments and colorants in components in paper products in contact with aqueous and fatty foods. The Food and Drug Administration in 1972 proposed the use of QA as a colorant for plastics which contact food. The use of these pigments, in particular, as colorants which contact ingestible food products, strongly suggests that these pigments do not pose human health or environmental concerns.

Sediments Summary

The appended physical, chemical, and toxicological data support Du Pont's position that the pigment-colored sediments along the riverbank do not pose a current human health or environmental risk. Likewise, the long-term stability of these pigments precludes future risk to human health and the environment due to the lack of degradation in the environment. Therefore, Du Pont neither sees any need nor proposes to further evaluate the presence of the pigment-colored sediments observed along the riverbank.

Historical Aerial Particulates Deposition

During the operational history of the Newport facility, residents living near the facility have complained about air emissions problems including particulates and odor. As requested by the EPA, Du Pont has investigated this concern for particulate emissions. Three categories of emissions have been identified: one time events which drew immediate attention by the public (i.e., blue dog event); historical controlled aerial emissions from the operational facilities; and wind blown dust from the plant area.

The single events resulted in immediate Du Pont response and clean-up precluding present day identification of residual particulates by sampling.

The controlled air emissions and wind blown dust are expected to have resulted in deposition in the direction of prevailing winds. The wind-rose diagram presented in the Data Sufficiency Memorandum (WCC, April 1989), shows that the prevailing winds at the Newport Site blow toward the northwest to west-northwest during most of the year. Therefore, soil sampling would have to be conducted northwest to west-northwest of this facility.

In order to collect a soil sample that most accurately represents historical aerial deposition, the sampling area must have remained undisturbed since the period of emissions. Our review of the aerial photographs dating back to 1937 suggest that there are no undisturbed areas immediately adjacent to the Newport Site or extending outwards for at least 2,500 feet in the prevailing wind direction. Furthermore, as we move farther away from the facility, the impact from other potential sources complicates the interpretive value of soil data. Therefore, there are no known nearby undisturbed areas where soil samples can be taken to most accurately represent historical air emissions of particulates from the Newport Site.

Du Pont feels, however, that there is a possible solution to this sampling dilemma. Soil samples have recently been collected from central areas and along the boundaries of the tract of land owned by Du Pont which is adjacent to the Site and used by Newport residents as a ball park. This ball park lies in the direction of the prevailing winds from the Newport Site. While the central portion of this area has been disturbed by temporarily converting the ball field into a gravel parking lot during the 1950's, the perimeter of the parcel may represent undisturbed soil conditions dating back to the era of Lithopone operations.

Du Pont has documented land use practices for this area which will allow effective interpretation of the soils data. Du Pont also feels confident that its knowledge of historic land use for the ball park will be supported by an evaluation of the distinct lithological changes of the soil profiles observed during soil sampling in the central area that correspond to known changes of land use supported by aerial photography. If the analytical results from the soil profiles indicate no disturbance, then these samples will best represent the impact of particulate emissions from the Newport operations on the neighborhood.

Thus, the ball park represents the only feasible off-site soil sampling location in the direction of the prevailing winds. The results of the ball park soil sampling will be presented in the Phase III Data Sufficiency Report. Therefore, Du Pont neither sees a need nor proposes to conduct any further investigation of the historical air emissions concerns.

If you have any questions, please do not hesitate to contact me. I await your confirmation on these issues.

Sincerely,

Joel Karmazyn
Project Manager

JK/mlm

3-11RPT.JK

Attachment

cc: K. Kalbacher, DNREC
N. Griffiths, Du Pont
C. Trmal, Du Pont
B. Butler, i.e., B. De Stefano, Du Pont
F. Hannigan, Ciba-Geigy
R. Gresh, WCC

March 12, 1991
Project No: 400754

APPENDIX A

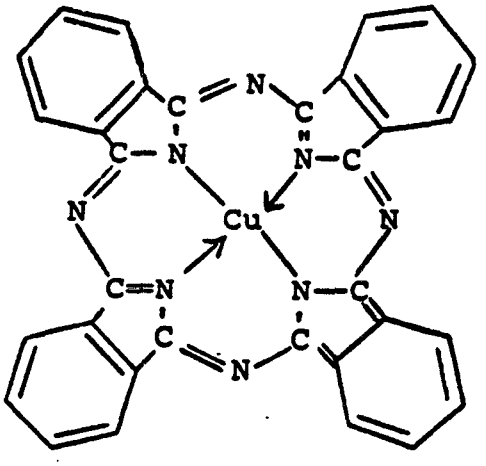
CPC

HASKELL LABORATORY

LIMITED DISTRIBUTION

This review reflects the available toxicity literature, both published and unpublished. Studies have not been evaluated for scientific merit.

Common Name: Phthalocyanine Blue
Chemical Name: Copper, (29H, 31H-phthalocyaninato(2-)-N(29), N(30), N(31), N(32))-(SP-4-1)-
Synonyms: Copper phthalocyanine, Monastral® Blue, C.I. 74160, KP-4, C.I. Pigment Blue 15, CPC
CAS Registry No.: 147-14-8
Chemical Structure:



Physical Properties: (2)

Description	:	Blue solid
Molecular Weight	:	576.1
Boiling Point	:	----
Melting Point	:	Decomposes
Density/Specific Gravity	:	1.5-1.7
Vapor Pressure	:	----
Flash Point/Flammability	:	----
Explosive Limits	:	----
Solubility	:	Insoluble in water
Conversion Factors	:	----

Exposure Standards

None

DOT Classification

None

EPA RCRA Status

None

FDA Status

Phthalocyanine Blue is cleared under 21 CFR for the following food-related uses:

Cleared for use as a pigment and colorant under §175.300 (resinous and polymeric coatings), §175.380 (xylene-formaldehyde resins condensed with 4,4' isopropylidenediphenol epichlorohydrin epoxy resins), §175.390 (zinc-silicon dioxide matrix coatings), §176.170 (components of paper and paperboard in contact with aqueous and fatty foods), §177.1210 (closures with sealing gaskets for food containers), §177.1350 (ethylene-vinyl acetate copolymers), and §177.1460 (melamine-formaldehyde resins in molded articles).

Cleared for use as a pigment under §177.1680 (polyurethane resins).

Phthalocyanine Blue (C.I. Pigment Blue 15, C.I. No. 74160) cleared under §177.2260 (filters, resin-bonded) for use at levels not to exceed 0.1% in thermoplastic adhesives fabricated from ethylene-vinyl acetate copolymers complying with §177.1520 (olefin polymers) (FR Jan. 9, 1969).

Cleared for use as a color under §177.2600 (rubber articles intended for repeated use), with total colors not to exceed 10% by weight of rubber product.

Petition withdrawn Dec. 30, 1966, would have cleared rigid polyvinyl chloride sheeting colored with copper phthalocyanine (phthalocyanine blue) or copper phthalocyanine, polychlorinated.

Petition withdrawn March 6, 1968, would have cleared Pigment Blue 15 (Phthalocyanine Blue, C.I. No. 74160, for use as a component of polyolefin food-contact articles.

FDA proposal June 6, 1972 would delete clearance under §177.1680 (polyurethane resins) and would clear use of C.I. Pigment Blue (C.I. No. 74160) under an order for colorants for plastics.

TSCA Inventory

Yes

TOXICITY

Summary

Copper phthalocyanine (CPC) has very low acute oral toxicity with no deaths or clinical signs of toxicity in rats administered up to 17 grams/kg. Contact of the pigment with the skin of guinea pigs under an impervious cover for 24 hours produced only slight irritation and no evidence of absorption through the skin. Additionally, no evidence of sensitization was seen. While no information is available on its carcinogenic or embryotoxic potential, CPC was not mutagenic in the Ames bioassay.

A. Acute

1. Oral

- Monastral® Blue BT-284-D was administered by intragastric intubation as a suspension in peanut oil to ten male rats in a single dose of 17,000 mg/kg. Survivors were sacrificed 14 days after. None of the rats died nor exhibited clinical signs of toxicity. Since the feces were stained blue for a few days after dosing, the pigment probably passes through the gastrointestinal tract without absorption (2).

- A single dose of 1000 mg/kg of MDD-1040 (90% copper phthalocyanine, 10% dichlorostannic phthalocyanine) as a suspension in olive oil was administered to a single rat by stomach tube. During a ten-day observation period, no ill effects were observed and at autopsy no pathology nor trace of pigment was discovered (2).

- No deaths occurred in a group of rats and mice administered 3200 mg/kg (1).

- A commercial pigment, Monastral® Fast Blue RDC paste, which contains 20% CPC as its active ingredient, did not cause any deaths when administered to a group of ten rats at a dose of 25 grams/kg (2).

2. Skin

- Application of solid phthalocyanine blue to guinea pig skin under an impervious covering for 24 hours caused only slight irritation with no evidence of skin penetration. Additionally, no evidence of sensitization was found (1).

- A patch of Dacron® fabric containing 0.02% Uvitex® 1159 and 1 ppm Monastral® Blue-B did not produce irritation or sensitization in any of the 210 human subjects exposed (2).

- Blue color-sealed Orlon® yarn containing Monastral® Blue BT 284-D, Thiofast Red, Excelsior carbon black and titanium dioxide produced neither primary irritation nor allergic sensitization in 197 persons tested (2).

3. Eyes

No information available

4. Inhalation

No information available

5. Intraperitoneal Injection

- LD50 (rats) = 400-800 mg/kg (1).

- LD50 (mice) = 200-400 mg/kg (1).

B. Extended Studies

1. Oral

- MDD 1040 (90% copper phthalocyanine, 10% dichlorostannic phthalocyanine) in olive oil was administered by stomach tube to five rats at a dose of 200 mg/kg five times per week for two weeks. The rats were killed three days after the final dose. The color of the feces indicated that most of the chemical was excreted without gastrointestinal absorption. During the treatment period activity was normal; however, a transient weight loss occurred. At autopsy no pathology nor trace of pigments in the organs was noted (2).

2. Subcutaneous Injection

- No tumors were found in a group of 20 mice injected subcutaneously with 0.5 mg of CPC once a week, for eight months. Seventeen of the 20 mice survived the study (3).

C. Carcinogenic Potential

- No life-time studies are available. While no tumors were found in an eight-month injection study (3), the study is limited for assessing the carcinogenic potential of CPC.

D. Mutagenic Potential

- Monastral®Blue BT-284D (concentrations up to 100 µg/plate) was not mutagenic in Salmonella typhimurium tester strains TA 1535, TA 1537, or TA 1538 either in the presence or absence of a liver microsomal activation system (2).

- 0.01 mg copper phthalocyanine dissolved in 0.01 ml DMSO was tested in the Ames assay with and without liver homogenate. The compound was not mutagenic (4).

E. Embryotoxic Potential

No information available

F. Other Reproduction Studies

None

G. Aquatic/Environmental Studies

- See Related Reference 5

H. Human Exposure

- The Medical Division of the Chambers Works (Du Pont) reported several years ago that during an incident of severe contamination of the skin of workers using Monastral®Blue,no irritation or sensitization of the skin, nor irritation of mucous membranes, or systemic injury was observed during this incident or during the 15 years of manufacture (2).

I. Epidemiology

No information available

J. Metabolism

No information available

K. Biochemical Studies

No information available

REFERENCES

1. Eastman Kodak Company Data (3/6/74).

2. Du Pont Company Data, Haskell Laboratory.

3. Haddow, A. and E. S. Horning, J. Natl. Cancer Inst., 24: 109-147.

4. Milvy, P. and Kay, K., J. Toxicol. Environ. Health, 4(1): 31-36 (1978).

RELATED REFERENCES

Environmental Studies

5. Holland, F. S. and H. Rolskov, Proc. Effluent Water Treat. Conv., No. 9, 1-6 (1978) (CA92:185300).

"The treatment of metal-bearing toxic wastes by a new electrochemical system"

N. J. Hunt:mdc
May 25, 1976

Updated by:
Pamela J. Gort:md
January 20, 1978

Updated by:
Linda J. VerNooy
January 28, 1980

Updated by:
Richard C. Graham:mjh
February 15, 1983

R. C. Graham

March 12, 1991
Project No: 400754

APPENDIX B

QA

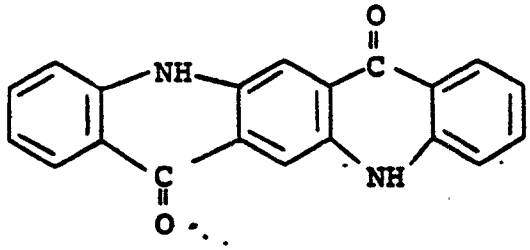
DUPONT

HASKELL LABORATORY

LIMITED DISTRIBUTION

This review reflects the available toxicity literature, both published and unpublished. Studies have not been evaluated for scientific merit.

Common Name: C. I. Pigment Violet 19
Chemical Name: Quino (2,3-b) acridine-7,14-dione, 5-12-dihydro-(8CI, 9CI)
Synonyms: Cinquasia Red
Cinquasia Red B
Cinquasia Red Y
Cinquasia Violet R
Fastogen Super Red BN
Hostaperm Red E 3B
Hostaperm Red Violet ER
Monastral Red B
Monastral Red Y
Monastral Violet R
Pigment Pink Quinacridone S
PV Fast Red E 3B
PV Fast Red E 5B
Quinacridone
Quinacridone Violet
CAS Registry No.: 1047-16-1
(Old No. 67053-84-3)
Chemical Structure: (5)



Physical Properties: (5)

Solubility : Insoluble in aliphatic petroleum, cellosolve, esters, ethanol, ketones, NC solvents, and xylene

Physical Properties (cont.):

Heat Stability : Stable to 165°C (stoving enamel)
Molecular Weight: 312.33

Exposure Standards:

None found

DOT Classification:

None found

FDA Status:

Quinacridone is cleared under 21 CFR for the following food-related uses:

Quinacridone Red

FDA proposal June 6, 1972, would clear C.I. Pigment Violet 19 (C.I. No. 46500) under an order for colorants for plastics only in olefin polymers complying with §177.1520 (olefin polymers), provided that the olefin polymer in the finished form in which it is to contact food when extracted by a method available on request from FDA shall yield not in excess of 0.006 ppm of the colorant (9).

TOXICITY

A. Acute

1. Oral

- ALD (rats) = > 7,500 mg/kg (1,2)
- LD50 (rats) = > 11,000 mg/kg (2)

2. Skin

- Comedo-producing reactions were noted in rabbit ears following treatment with C.I. Pigment 7 and C.I. Pigment 19 (8).
- At a concentration of 10%, Quinacridone Red was mildly irritating to the intact skin of five of ten guinea pigs and slightly more irritating to abraded skin. No evidence of a sensitization potential was noted (1).
- C.I. Pigment Violet 19 caused slight irritation on shaved intact rabbit skin after a 24-hour application. No irritation was noted after 48 hours (6).

3. Eyes

- No ocular effects were observed in treated rabbit eyes following instillation of C.I. Pigment Violet 19. An eye treated and promptly washed showed mild conjunctival irritation. The washed eye was normal one day after treatment (7).

4. Inhalation

No data found

B. Extended Studies

No data found

C. Carcinogenic, Mutagenic or Embryotoxic Potential

- Quinacridone Red was tested in Salmonella typhimurium strains TA 1535, TA 1537 and TA 1538 and found to be nonmutagenic either in the presence or absence of a liver microsomal activation system (3,4).
- No information was found on the carcinogenic or embryotoxic potential.

D. Other Reproduction Studies

No data found

E. Aquatic Studies

No data found

F. Human Exposure

- C.I. Pigment Violet 19 and C.I. Pigment Red 7 were implicated in acne-like skin changes in humans. A child's cheeks showed acne-like changes after they were colored with a red felt-tip pen. Numerous comedones appeared around a red tattoo colored with felt-tip pen ink in a 16-year-old girl (8).

G. Epidemiology

No information found

H. Epidemiology

No information found

I. Metabolism

No information found

REFERENCES

1. Du Pont Company, Unpublished Data, Haskell Laboratory

2. Du Pont Company, Unpublished Data, Haskell Laboratory

3. Du Pont Company, Unpublished Data, Haskell Laboratory

4. Du Pont Company, Unpublished Data, Haskell Laboratory

5. Amer. Assoc. of Textile Chemists and Colorists, and Society of Dyers Colour Index 3:3338 (1971).

6. Du Pont Company, Unpublished Data, Haskell Laboratory

REFERENCES (cont.)

7. Du Pont Company, Unpublished Data, Haskell Laboratory

8. Franz, E., et al., Z. Hautkr., 57(9):655-661 (1982) (TOXBIB82:201464).

9. Food Chemical News Guide, 381(19).

RELATED REFERENCES

Decomposition

10. Jones, F., et al., J. Soc. Dyers and Colourists, 91(11): 361-365 (1975) (World Textiles 7508609-7509550).

"Thermal stability of linear trans-quinacridone pigments"

Review

11. Anon - Cosmet. Toilet., 94(5):19 (1979).

"Violet #19 - potential new cosmetic color"

George T. Hall

George T. Hall:mjh
February 22, 1983

REVISED REPORT

E. I. du Pont de Nemours and Co., Inc.
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P. O. Box 50,
Newark, Delaware 19711

HASKELL LABORATORY REPORT NO. 746-82

Material Tested*	Haskell No.
Quino[2,3-b]acridine-7,14-dione, 5,12-dihydro-	14,653

Study Initiated/Completed
9/23/82-10/27/82

INHALATION APPROXIMATE LETHAL CONCENTRATION (ALC) OF MONASTRAL® RED Y RT-759-D

Summary: Groups of six male rats were exposed for four hours to atmospheres containing Monastral® Red Y RT-759-D at concentrations up to 3.1 mg/L. About 22% of the suspended atmospheric dust was <13 um aerodynamic diameter. No animals died during the exposures or up to two weeks later. The Approximate Lethal Concentration is therefore greater than 3.1 mg/L. Other than transient weight losses there were no significant clinical signs of toxicity observed.

Procedure

Animals: Groups of 6 male Crl:CD® rats, 7-8 weeks old and weighing between 226 and 250 grams, were placed in metal restrainers and exposed head-only for single 4-hour periods to atmospheres containing Monastral® Red Y RT-759-D. All rats were weighed and observed daily for 14-days post exposure, weekends not included.

Rats were housed in pairs in 8" x 8" x 14" stainless steel wire mesh cages. Purina Certified Rodent Chow® #5002 and water were available ad libitum. Rats were weighed and observed for general suitability for 1 week prior to test.

Atmosphere Generation: Dust atmospheres of Monastral® Red Y RT-759-D were generated with a vertical two-stage glass generator consisting of a dust reservoir and a cyclone elutriator. An electric stirring motor and steel rod with plastic paddles agitated dust in the generator. Air introduced at the reservoir carried dust particles upward to the elutriator. Additional houseline air carried airborne dust into the chamber.

Analytical: Chamber atmospheres were analyzed gravimetically at 30-minute intervals. Calibrated volumes of test atmosphere were passed through preweighed glass fiber filters (Gelman Type AE, 25 mm) and atmospheric concentrations determined from filter weight gain. Airborne particle size measurements were obtained using a Sierra 8-stage cascade impactor.

Results:

TABLE 1

Chamber Dust Concentration (mg/L)			% Respirable Dust (<13 um aerodynamic diameter)	Fractional Mortality # Deaths/ # Exposed
Mean	S.D.	Range		
1.5	1.3	0.8 - 5.5	12	0/6
1.6	1.8	0.0 - 6.1	17	0/6
2.4	2.0	0.9 - 6.9	N.D.**	0/6
2.6	2.5	0.4 - 6.8	N.D.**	0/6
3.1	2.8	1.1 - 10	21	0/6

**Particle size not determined.

No rats died when exposed to 3.1 mg/L of Monastral® Red Y RT-759-D dust (or any of the lower concentrations). This was the highest concentration which could be maintained in the chamber atmosphere with this generation method. Although the original particle size of this dust is considerably smaller, only about 22% of the airborne particles were less than 13 um aerodynamic diameter. Particles of 10 um or less are considered of

respirable size. The increased particle size in these experiments is likely due to formation of agglomerates in the dust generator. Use of dust which had been vacuum dried at 60°C did not significantly increase the amount of respirable dust generated.

Animal Observations: Rats exposed to Monastral® Red Y RT-759-D dust showed a mild weight loss immediately after exposure but resumed a normal weight gain rate two days later. After exposure all rats had red stained fur.

---

* CAS Registry No.: 1047-16-1

Purity: 95%

Contaminants: Dihydroquinacridone (QA) and quinacridonequinone (QAQ)

Work and Report by: Keith A. Jervey
Keith A. Jervey
Laboratory Assistant

David T. Kelly
Toxicologist

Study Director: Bruce A. Burgess
Bruce A. Burgess
Research Toxicologist

Approved by: Gerald L. Kennedy, Jr.
Gerald L. Kennedy, Jr.
Section Supervisor
Acute Investigations

Date Issued: January 3, 1983
Date Reissued: May 7, 1984

Haskell Lab. Report No. 746-82

E. I. du Pont de Nemours and Co., Inc.
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P. O. Box 50,
Newark, Delaware 19711

HASKELL LABORATORY REPORT NO. 24-83

Material Tested*	Haskell No.
Quino[2,3-b]acridine-7,14-dione, 5,12-dihydro-	14,654
Quino[2,3-b]acridine-7,14-dione, 5,12-dihydro-	14,655

Study Initiated/Completed	Material Submitted by
12/27/82-1/7/83	Don Yonker Chemicals & Pigments Department Chestnut Run

SKIN IRRITATION TEST ON RABBITS

Summary: Monastral® Red B RT-790-D moistened with distilled water (H-14,654), Monastral® Violet R aqueous dispersion RW-767-P as received (H-14,655)

, caused no irritation on the intact skin of rabbits in 24, 48 or 72 hours after treatment. Although no skin irritation was seen with these materials, good industrial hygiene practice would be to wash with soap and water if contact occurs.

Procedure: Twelve male albino rabbits were clipped free of hair on the trunk and lateral area and were placed in stocks. Doses of 0.5 mL of the test material (as received) or 0.5 g. slightly moistened with discilled water were applied to intact skin under 1 1/2" x 1 1/2" 12-ply gauze squares. A rubber sheet was then loosely wrapped around the trunk of each rabbit and secured with adhesive tape. After 24 hours, the rubber sheets were unwrapped, the sites outlined with indelible ink and the gauze pads removed. Test sites were then evaluated, the rabbits removed from the stocks and the sites washed. Observations were also made at 48 and 72 hours.

Results:

	24-Hour Observation		48-Hour Observation	
	Erythema	Edema	Erythema	Edema
H-14,654	6/6 None	6/6 None	6/6 None	6/6 None
H-14,655	6/6 None	6/6 None	6/6 None	6/6 None

	72-Hour Observation	
	Erythema	Edema
H-14,654	6/6 None	6/6 None
H-14,655	6/6 None	6/6 None

H-14,654

Purity: 88%

Contaminant: Quinacridonequinone

Synonyms:
- Monastral® Red B RT-790-D
- Quinacridone red pigment

H-14,655

Purity: 15.0% Pigment

Contaminant: Sodium tetraborate

Synonym: Monastral® Violet R aqueous dispersion RW-767-P

Report by: Lonnie Hinckle
Lonnie Hinckle
Technician

Reviewed by: O. Louis Dashiell
O. Louis Dashiell
Study Director

Approved by: Gerald L. Kennedy, Jr.
Gerald L. Kennedy, Jr.
Section Supervisor
Acute Investigations

Date Issued: February 7, 1983

Haskell Lab. Report No. 24-83

E. I. du Pont de Nemours and Co., Inc.
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P. O. Box 50,
Newark, Delaware 19711

HASKELL LABORATORY REPORT NO. HLO 397-83

Material Tested*	Haskell No.
Quino[2,3-b]acridine-7,14-dione, 5,12-dihydro-	14,943

Study Initiated/Completed
8/11/83 - 8/20/83

SKIN IRRITATION TEST ON RABBITS

Haskell Evaluation: Haskell Standard Operating Procedure for skin irritation testing was followed with this exception: due to difficulty in forming a suspension the material was applied as 0.5 mL of a 0.5 g/mL mixture, for a total dose of 0.25 g. Although a smaller area of skin would be covered than if 0.5 g had been used, this is not judged to have affected the severity of response or the outcome of the study. Monastral® Transparent Red Y RT-218-D produced slight to mild erythema and no edema when patches were removed at 24 hours. Responses cleared or decreased to slight when the study was terminated at 48 hours. When tested according to this procedure Monastral® Transparent Red Y RT-218-D is a mild skin irritant.

* Synonym: Monastral® Transparent Red Y RT-218-D

Purity: >90%

Contaminants: Traces of the following:

Na^+

H^+

5,6,12,13-Tetrahydroquino[2,3-b]acridine-7,14-dione

4,11-Dichloro-5,6,12,13-tetrahydroquino[2,3-b]acridine-7,14-dione

Quinacridonequinones

Report by: Carol S. Auletta
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Date Issued: October 7, 1983
Haskell Lab. Report No. HLO 397-83
Appendix attached: 8 pp., Bio/dynamics Project 4577-83
Total pages in this report: 10

Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO.: 4577-83

PRIMARY DERMAL IRRITATION STUDY IN RABBITS
(Haskell Skin Irritation Test)

TEST MATERIAL: H #14,943

Submitted to: E.I. duPont de Nemours & Company
Newark, Delaware

Date: September 26, 1983

I. INTRODUCTION

This study was conducted for E.I. duPont de Nemours & Company to evaluate the primary dermal irritation produced by by H #14,943. The study was performed at Bio/dynamics, Inc., Mettlers Road, East Millstone, New Jersey 08873.

This report has been reviewed by the Quality Assurance Unit of Bio/dynamics, Inc. to assure its conformance with the protocol and the raw data.

II. DATES OF STUDY

Animal Receipt:	July 5, 11 and 25, 1983
Initiation (Dosing):	August 17, 1983
Termination (Last Observation):	August 20, 1983

III. STUDY PERSONNEL

Study Director:	Carol S. Auletta, B.A., D.A.B.T.
Laboratory Supervisor:	Donna L. Blaszcak, B.S., AALAS, L.A.T.
Technician-in-Charge:	Janet Erickson, A.A.S., AALAS, L.A.T.
Study Monitor (Report Preparation):	Antoinette S. Jones

IV. MATERIALS

A. Test Animals:	Albino Rabbits
Breed:	New Zealand White
Reason for Selection:	Standard laboratory animal for dermal irritation studies. The New Zealand White breed was used because of its availability and because of the existing historical data base for comparative evaluation.
Supplier:	Hazleton-Dutchland, Inc. Denver, Pennsylvania
Number:	Six (3 males, 3 females)
Age:	Young adults

IV. MATERIALS (cont.)

Weight (Preterm):	2.6 to 3.2 kilograms
Equilibration Period:	23, 37 and 43 days
Husbandry:	Currently acceptable practices of good animal husbandry were followed, e.g., Guide for the Care and Use of Laboratory Animals; DHEW Publication NO. (NIH) 78-23 Revised 1978..
Housing:	Individually housed
Cages:	Suspended, stainless steel with wire mesh bottoms.
Environmental Conditions:	Temperature: 60-70°F is considered an acceptable temperature range for rabbits; room temperature was monitored twice daily and maintained within this range to the maximum extent possible. Humidity: 30-70% is considered an acceptable humidity range for rabbits; room humidity was monitored and recorded daily and maintained within this range to the maximum extent possible. Light Cycle: 12 hours light, 12 hours dark (controlled by an automatic timer).
Food:	Lab Rabbit Chow HF (Purina #5326), ad libitum.
Water:	Automatic watering system, ad libitum Municipal water supply (Elizabethtown Water Co.)
Identification:	Each animal was identified with a monel ear tag bearing a unique number prior to testing.
Selection:	Animals were randomly placed in cages upon receipt and were placed on study as available at the time of study initiation. Animals considered unsuitable for study because of poor health, unacceptable skin, or outlying body weights were excluded from selection.

IV. MATERIALS (cont.)

B. Test Material: H #14,943

Description:	Red Powder
Date of Receipt:	July 28, 1983
Received from:	E.I. duPont de Nemours & Company
Storage:	Room temperature

V. METHODS:

A. Preparation of Test Material:

The test material was mixed with physiological saline to achieve a 0.5 gram/ml mixture.

B. Preparation of Animals:

On the day before dosing, (approximately 18 hours prior to dosing) the hair of each rabbit was closely clipped from the back with an electric clipper, so as to expose the back from the scapular to the lumbar region. No abrasions were made, i.e., the skin of all animals remained intact.

C. Administration of Test Material:

There was one test site on the back of each animal. Five-tenths milliliter (0.5 ml) of the test material mixture was applied to each site beneath a surgical gauze square, 1"x1", eight single layers thick. The gauze was placed directly on the test site and held in place with tape. Polyethylene sheeting was then wrapped around the animal and secured with tape to retard evaporation and keep the test material in contact with the skin without undue pressure. Elizabethan collars were placed on each animal to prevent them from disturbing the wrapping and test sites.

Following 24 hours of exposure, the polyethylene sheeting was loosened, the skin at the corners of the gauze squares was marked with a waterproof pen, and the wrappings and gauze squares were removed. The skin at the test site was gently washed with castile soap and warm water. The skin was rinsed with water and patted dry with paper toweling and the animal returned to its cage. After approximately 30 minutes, dermal observations were made.

VI. EXPERIMENTAL EVALUATION (In-Life):

Viability Check: Twice Daily

Evaluation of Skin Irritation:

1. Intervals:

24.5 and 48 hours after application.

2. Methods:

At each interval all sites were evaluated for erythema and edema or other evidence of dermal irritation according to the Draize scoring system. Adjacent areas of untreated skin were used for comparison. Special notations were made of necrosis, eschar, or other evidence of irreversible tissue structure.

VII. RAW DATA STORAGE:

All raw data, the original study protocol and final report will be retained on file in the Bio/dynamics Archives.

VIII. RESULTS AND DISCUSSION

Dermal observations are presented in Table I; the scoring system used is presented in Appendix A. H #14.943 produced mild, transient dermal irritation. All animals exhibited very slight or well-defined erythema, with no edema, at 24 hours. At 48 hours, two of the six animals were free of irritation and four exhibited very slight erythema only. There was no evidence of tissue destruction or corrosivity.

Carol S. Auletta, B.A., D.A.B.T.
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9/23/83
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Date

TABLE I

DOT SKIN CORROSION TEST IN RABBITS

TEST MATERIAL: H #14,943

INDIVIDUAL DERMAL IRRITATION SCORES[a]

Time Interval	Patch Sites & Observations		Animal Number and Sex					
			1695M	1700F	1721M	1776F	1839M	1840F
24 Hours	Left Front	ER	2	1	1	1	2	1
		ED	0	0	0	0	0	0
48 Hours	Left Front	ER	1	0	0	1	1	1
		ED	0	0	0	0	0	0

[a]Scored using scale presented in Appendix A.
M-Male
F-Female
ER-Erythema
ED-Edema

APPENDIX A

DRAIZE[1] EVALUATION OF DERMAL IRRITATION

Dermal Observations

Erythema and Eschar Formation (Most severely affected area graded):

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness)	4
Eschar formation	4E
Necrosis	4N

Edema Formation (Most severely affected area graded):

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4

[1]Draize, J.H. 1959. The Appraisal of Chemicals in Foods, Drugs, and Cosmetics, pp. 36-45. Association of Food and Drug Officials of the United States, Austin, Texas.

March 12, 1991
Project No: 400754

APPENDIX C

Barium

Patty's Industrial Hygiene and Toxicology

THIRD REVISED EDITION

Volume 2A
TOXICOLOGY

GEORGE D. CLAYTON
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1981

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4 BARIUM, Ba

4.1 Sources and Production (1)

Barite, natural barium sulfate ($BaSO_4$), occurs in the United States in Alaska, Arkansas, California, Georgia, Missouri, Nevada, and Tennessee, and in Canada and

Mexico, and was produced at 38 mines in the seven states in 1973, with Nevada supplying 50 percent of the tonnage. Missouri ranked second. Domestic production was 1,104,000 short tons in 1973, representing 23 percent of world production. U.S. imports totaled 716,000 short tons, and exports of $BaSO_4$ and $BaCO_3$, about 68,000 short tons.

$BaSO_4$ is produced from high grade ore (75 to 98 percent) often in association with granite and shale, crushed, beneficiated by froth flotation or by jigging, and dried. $Ba(OH)_2$ can be made directly from barite ore. Further details on sources and production may be found in Reference 1.

4.2 Uses and Industrial Exposures

About 90 percent crude barite is used in manufacture of ground barite, the remainder for lithopone (28 percent ZnS, 72 percent $BaSO_4$) and Ba chemicals. Oil- and gas-well drilling, the largest use of ground barite, accounts for 95 percent of the total output. The glass, paint, and rubber industries consume crushed and ground barite. The amount of barite used for lithopone is decreasing owing to competition from TiO_2 as a paint pigment. A barium titanate ceramic has been patented, as well as a process for barium titanate crystals. A rubber–barite mixture for road construction, vehicle undercoats, and roofing paints has been patented, using particles 90 percent less than 10 μ diameter. Barium chemicals of greatest domestic industrial importance are the carbonate, chloride, hydroxide, sulfate, and nitrate (166). Barium metal is used as a "getter" to remove gases from vacuum tubes. Barium–aluminum alloys are also used as getters.

4.3 Physical and Chemical Properties

The physical and chemical properties of Ba and some of its more industrially important compounds are listed in Table 29.4.1.

Barium, a silver-white metal obtained from the electrolysis of the molten chloride, is one of the less expensive metals that have the distinctive properties of absorbing gases. Barium is highly electronegative, liberating H_2 actively from cold water. Barium sulfate is the source of most Ba compounds. When $BaSO_4$ is reduced to the sulfide and treated with $ZnSO_4$ an insoluble mixture of $BaSO_4$ and ZnS, lithopone is formed; for use as a paint pigment, it is given a heat treatment. Barium fluoride (BaF_2), made from $BaCO_3$, is used as a flux to lower the melting point of some salt mixtures in joining metals.

Table 29.4.1. Physical and Chemical Properties of Ba and Some of Its Compounds

Form of Ba	At. or Mol. Wt.	Sp. Gr.	M.P. (°C)	B.P. (°C)	Solubility
Barium (Ba)	137.36	3.5 (20°C)		1640	Dec. with evoln. of H_2; sol. alcohol; insol. C_6H_6
Barium sulfate ($BaSO_4$)	233.43	4.5 (15°C)		Tr.[a] 1149 monocl	2.46 mg/liter (25°C), 4.13 mg/liter (100°C); sl sol HCl H_2SO_4

4.4 Analytic Determination

The spectrographic method of Grabowski and Unice (167) is applicable to air samples and samples of biologic origin that are soluble in HCl following appropriate fusion or acid digestion. A general analytic procedure for metals involving atomic absorption spectrometry is described in Reference 168. For Ba, the detection limit is 1 to 25 ppm if the reducing nitrous oxide–acetylene flame is used.

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Form of Ba	At. or Mol. Wt.	Sp. Gr.	M.P. (°C)	B.P. (°C)	Solubility
Barium (Ba)	137.36	3.5 (20°C)	752	1640	Dec. with evoln. of H_2; sol. alcohol; insol. C_6H_6
Barium sulfate ($BaSO_4$)	233.43	4.5 (15°C)	1580	Tr.[a] 1149 monocl.	2.46 mg/liter (25°C), 4.13 mg/liter (100°C); sl. sol. HCl, H_2SO_4
Barium hydroxide [$Ba(OH)_2 \cdot 8H_2O$]	171.38	2.18 (16°C)	78	$-8H_2O$, 780	16.7 g/liter (0°C); 947 g/liter (100°C)
Barium carbonate ($BaCO_3$)	197.37	4.43	1740[b]	Dec.	20 mg/liter (20°C); 60 mg/liter (100°C); sol. acid, NH_4Cl; insol. alcohol
Barium chloride ($BaCl_2$)	208.25	3.86 (24°C)	Tr. to cub.	1560	375 g/liter (26°C), 590 g/liter (100°C); sl. sol. HCl, HNO_3; v. sl. sol. alcohol
Barium nitrate [$Ba(NO_3)_2$]	261.35	3.24 (23°C)	592	Dec.	87 g/liter (20°C), 342 g/liter (100°C); insol. alcohol; sl. sol. acid
Barium fluoride (BaF_2)	175.34	4.89	1355	2137	1.2 g/liter (25°C); sl. sol. hot water; sol. acid, NH_4Cl

[a] Tr. = transition.
[b] 90 atm.

4.5 Physiologic Responses

Compounds of Ba are highly toxic, unlike others in its chemical group, Ca and Sr. $BaCO_3$ has found use as a rat poison, and the sulfide as a depilatory. The fatal dose of $BaCl_2$ for man is reported (169) to be between 0.8 and 0.9 g (0.55 to 0.6 g as Ba).

4.5.1 Animal Toxicity

Fasekas et al. (170) have reported that a subcutaneous injection of $BaCl_2$ at 5 mg/kg caused acute toxicity and death of rabbits after 2 to 2.5 hr. Chronic poisoning was achieved by the repeated injection of 10, 5, and 2 mg/kg; the rabbits in this series were killed at 98 to 193 days. Effects on the central nervous system were described. For acute toxicity data of Ba compounds for laboratory animals by various routes of administration, consult the NIOSH Registry (171).

The symptoms of Ba poisoning are excessive salivation, vomiting, colic, diarrhea, convulsive tremors, slow, hard pulse, and elevated blood pressure. Hemorrhages may occur in the stomach, intestines, and kidneys. Muscular paralysis may follow. According to the dose and solubility of the Ba salt, death may occur in a few hours or a few days.

Truhaut et al. (172) reviewed the foreign literature on animal toxicity and contributed original observations on acute and chronic subcutaneous toxicity of $BaCl_2$ in guinea pigs. At toxic doses neighboring on the subcutaneous LD_{50} (19.3 mg/kg) no morphological changes specific to Ba^{2+} were observed, except possibly on the nervous system where degenerative changes were seen. At lower doses, 12 mg/kg subcutaneous daily, repeated for 26 weeks, a myeloid hyperplasia of the spleen, liver, and bone marrow developed which was reflected in cellular changes in the peripheral blood. The authors noted a remarkable adaptation and resistance of the guinea pigs to the daily administration of two-thirds of the LD_{50} in surviving for 26 weeks. The blood and hematopoietic organs at the end of the second week showed a considerable elevation of leukocytes in 28 of 32 guinea pigs, giving rise to a polychromatophilia that ended by the third week. Parallel to these changes, a frank myeloid reaction was manifest in the bone marrow. In the skeleton, the femur and inferior maxilla showed "condensing" osseous lesions in about half of the animals (173).

Douglas and Rubin (174) found that Ba, like Ca and Sr, can activate the secretion of catecholamines from the adrenal medulla, but unlike Ca and Sr, can activate without prior Ca deprivation. Barium probably acts on the chromaffin cell membrane by displacing Ca to make a more permeable membrane, resembling its action on smooth and cardiac muscle, providing stimulation and later paralysis of the central nervous system.

Barite dust inhaled by guinea pigs is claimed by Arrigoni (175) to result in nodular pulmonary granulation characteristic of human baritosis.

Bronchogenic carcinoma (squamous-cell type) developed in rats intratracheally injected with radioactive particles of $BaSO_4$ (^{35}S) (176).

4.5.2 Human Toxicity and Industrial Experience

A benign pneumoconiosis, baritosis, in workers exposed to finely ground $BaSO_4$, first described in Italy, was later confirmed by Arrigoni (175). Baritosis was later reported in the United States in barite miners by Pendergrass and Leopold (177), in Germany (178), and in Czechoslovakia (179). Baritosis also occurred among workers handling lithopone (180).

Baritosis causes no specific symptoms and no changes in pulmonary function. The radiological appearances are specific and due to the radiopacity of the sulfate; they are circumscribed nodules, larger and more numerous than silicotic nodules, and evenly distributed throughout both lung fields. These radiological opacities, particularly the nodulation, disappear in most cases upon cessation of exposure, but there often remain some signs of chronic bronchial irritation. Bronchial irritation has been reported in a factory where bomb casings were heated in $BaCO_3$ (181), and BaO dust is considered a potential agent for dermal and nasal irritation (182).

The only reports of poisoning from barium salts are from absorption from accidental ingestion, for example, an outbreak of gastroenteritis from $BaCO_3$, intended for rat poisoning, but placed in error in pastry flour (183). In addition to gastroenteritis, a slow pulse rate with extra systoles and symptoms of muscular paralysis occurred. In two other cases of $BaCO_3$ poisoning, hypokalemia with electrocardiographic recordings typical of such changes occurred (184). Animal experiments have confirmed potassium deficiency in Ba poisoning (185).

4.5.3 Metabolism

Ba in its soluble forms rapidly permeates the gastrointestinal tract into the bloodstream, from which it disappears practically completely in 24 hr (186). A study of the metabolism of Ba^{140} in rats showed 24-hr urinary and fecal excretions to be 7 and 20 percent, respectively; Ba was irreversibly deposited in the skeleton in trace amounts (176). Thus Ba metabolism differs from that of Ca in that it is excreted in greater amounts in the feces than in the urine.

Ba is also deposited in the muscles where it remains for the first 30 hr, thereafter decreasing slowly from the site. The lungs are also an important storage site, but very little is retained by the liver, kidneys, and spleen, and practically none by the brain, heart, and hair. Its incorporation into the bones is similar to that of Ca but at a faster rate ($<$ twofold) (187). Protein binding of ^{140}Ba averaged 54 percent of the administered dose, about 0.8 that of Ca, with Ba clearance increasing with saline infusion, indicating Ba clearance is related to Ca clearance as a power function (188).

The determination of Ba in human bone by radioactivation analysis showed no accumulation throughout a lifetime (7 ppm, ashed tissue) nor any accumulation in soft tissue as determined on 37 cadavers (11 to 24 ppm, ashed tissue). The pigmented parts of the eye, iris and choroid, contained more (25 ppm, wet tissue) than other parts of the eye

(189). Thus Ba differs strikingly from a heavier element in the group, Ra, which is a pronounced bone seeker.

4.5.4 Mode of Action

Ba stimulates all muscle, striped, unstriped, and cardiac, irrespective of innervation. Ba is mutually antagonistic to all muscular depressants (Ca). Ba produces strong vasoconstriction by direct stimulation of arterial muscle, violent stimulation of smooth muscle (peristalsis), and stimulation followed by paralysis of the central nervous system. Hematopoiesis is reported stimulated in rabbits; toxic doses are hemolytic (190). The intimate mechanisms whereby these varied effects are produced are not understood.

4.6 Hygienic Standards of Exposure

The threshold limit of 0.5 mg Ba/m^3 of air was set by the American Conference of Governmental Industrial Hygienists on the advice of Edwin C. Hyatt, who had employed this limit without mishap for a few years in the control of exposures to $Ba(NO_3)_2$ at Los Alamos. It is not known what degree of safety this limit incorporates for dust exposures to more insoluble Ba compounds. This is the maximal permissible limit recommended in 1974 in the Soviet Union, and also by OSHA in 1978.

4.7 Flammability

The free metal presents a fire and explosion hazard if exposed to moist air owing to liberation of H_2.

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5 BERYLLIUM, Be

5.1 Source and Production (1)

Whereas beryl, BeAl silicate, used to be the main imported Be ore, bertrandite, Be silicate, mined in Utah, has now replaced beryl for one of the two domestic Be ore processing companies. Beryl, however, is still the source for the products of the second company. Bertrandite, though of extremely low Be content (<1 percent BeO compared with about 4 percent in beryl) is still preferred because of its far greater ease in extracting Be as the hydroxide, the near end product common to both ore processes.

The principal beryl-producing countries of the free world are Brazil, Republic of South Africa, Argentina, and Australia. The world production of beryl decreased from 8870 short tons in 1969 to 4290 in 1973; corresponding figures are not available for either domestic mined bertrandite or beryl.

U.S. exports of Be alloys, waste, and scrap consisting of Be lumps, single crystals, powder, Be-base alloy powder, and Be rods, sheet, and wire were mostly to Japan (60,400 lb) and West Germany (20,280 lb), with considerably lesser quantities to western European countries, Brazil, Canada, and Taiwan (1973).

Compared to the involved process for converting beryl to BeO outlined below, the conversion from bertrandite is essentially a less difficult three-step process of treatment with H_2SO_4 to form $BeSO_4$, alkalizing with NaOH to form $Be(OH)_2$, and heating to yield BeO. By comparison two processes, the fluoride and the sulfate processes, are used to convert beryl to BeO. The fluoride process involves sintering briquettes of a berylsodium ferric fluoride mixture, leaching the sintered briquettes with water, precipitating $Be(OH)_2$ with NaOH, filtering, and igniting the precipitate to form BeO. The sulfate process involves melting beryl at 1625°C, quenching the melt in cold water to obtain a glass, leaching with strong H_2SO_4, extracting $BeSO_4$ and $Al_2(SO_4)_3$ with water, and precipitating of the latter with $(NH_4)_2SO_4$. The $BeSO_4$ is precipitated as the hydroxide and ignited to form BeO. Beryllium metal is obtained by reducing BeF_2 with a stoichiometric deficiency of Mg. Excess BeF_2 acts as a flux permitting reaction at lower

March 12, 1991
Project No: 400754

APPENDIX D

Barium Sulfate

DUPONT

HASKELL LABORATORY

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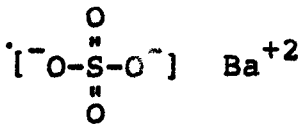
LIMITED DISTRIBUTION

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

Common Name: Barium Sulfate
Chemical Name: Sulfuric acid, barium salt(1:1)
Synonyms: C. I. Pigment White 121
CAS Registry No.: 7727-43-7
Chemical Structure:



Physical Properties:

Description:	White powder
Molecular Weight:	233.43
Boiling Point:	--
Melting Point:	1580°C
Density/Specific Gravity:	4.5 grams/mL @ 15°C
Vapor Pressure:	--
Flash Point/Flammability:	--
Explosive Limits:	--
Solubility:	Insoluble in water Slightly soluble in HCl and H_2SO_4
Conversion Factors:	--

Exposure Standards:

- AEL = 10 mg/m^3 (8-hour TWA)
- See Related Reference 39 for information on industrial handling of $BaSO_4$.

DOT Classification:

None

EPA RCRA Status:

None

AR306660

FDA Status:

- Exempted from tolerance requirements under §182.99 (adjuvants for pesticide chemicals) when used as a carrier in pesticide formulations applied to growing crops only (FR Sept. 2, 1975).
- Cleared under §175.105 (adhesives).
- Cleared as a pigment and colorant under §173.300 (resinous and polymeric coatings), §175.380 (xylene-formaldehyde resin condensed with 4,4'-isopropylidenediphenol epichlorohydrin epoxy resins) §175.390 (zinc-silicon dioxide matrix coatings), §176.170 (components of paper and paperboard in contact with aqueous and fatty foods), §177.1210 (closures with sealing gaskets for food containers) and §177.1350 (ethylene-vinyl acetate copolymers).
- Cleared as a pigment and colorant in melamine-formaldehyde resins under §177.1460 (melamine-formaldehyde resins in molded articles).
- Cleared as a filler employed in preparation of rubber articles under §177.2600 (rubber articles intended for repeated use).
- Petition withdrawn December 30, 1966, would have cleared indirect additive use of rigid polyvinyl chloride colored with barium sulfate in combinations with cadmium selenide, cadmium sulfide, zinc sulfide.
- FDA proposal June 6, 1972, would clear use under order for colorants for plastics.

TSCA Inventory:

Yes

TOXICITY

A. Acute

1. Oral

- A group of ten rats was administered 5000 mg/kg and then observed for 14 days. None of the rats died (8).
- $BaSO_4$ did not produce death in rats until the dosage reached 25-40% of their body weight. The cause of death at the higher dosages was stomach rupture or bowel obstruction. The LD50 producing death by bowel obstruction was 364 grams/kg. It is very unlikely that $BaSO_4$ could produce acute toxicity after a single oral dose (1).
- See Related References 23-26 for additional information.

2. Skin

No information found.

3. Eyes

- Injected experimentally into the anterior chamber of eyes of rabbits, a fine dispersion of $BaSO_4$ attracts many leukocytes, causes much hyperemia of the iris, dilation of perilimbal vessels, and clouding and vascularization of the cornea (11).
- The conjunctiva and eyelids of children have been accidentally injected with $BaSO_4$ after breaking open golf balls whose centers contained $BaSO_4$ under very high pressure. This material was reported to be remarkably inert causing little injury, with mainly a macrophage reaction evident microscopically (11).

4. Inhalation

- Groups of three beagle dogs that inhaled $BaSO_4$ or heat-treated $BaSO_4$ aerosols were studied for respiratory tract retention of the radioactive barium for 16 days. Initial fecal excretion was about 10% of the administered dose and decreased over the 16-day period to about 1% in the heat-treated $BaSO_4$ dogs and less than 0.5% in the $BaSO_4$ dogs. Lung retention leveled off at about 10% by

the fifth day post-exposure in the $BaSO_4$ dogs but was much higher in the heat-treated $BaSO_4$ dogs. Blood and urine levels were initially near 1% and dropped off only slightly over the 16 days for both $BaSO_4$ samples (7).

- Dogs inhaled an aerosol $BaSO_4$ with a particle size of about 0.5 um. The half-life for pulmonary clearance was eight days (41).

- $BaSO_4$ particles, whose mean size was 3.6 microns, were intratracheally injected into three groups of rats at dose levels of 23.3, 223 and 2330 micrograms. The rats were serially sacrificed over a 21-day period and the $BaSO_4$ left in the lung was determined. The 2330 microgram dose had a deep respiratory tract retention half-time of 27.5 days while the other doses had clearance half-times of about ten days (5). An earlier experiment had showed a half-life of about two days. The chief route of elimination was up the bronchial tree followed by swallowing and subsequent elimination via the urine and feces (3).

- After the intratracheal injection in rats of radiolabeled $BaSO_4$ particles, only 80% were rapidly removed from the distal trachea by mucociliary clearance. Some 20% were cleared with a mean half-life of 16 hours. Approximately 1% remained in the tracheal tissue for at least 30 days (17).

- A group of 12 rats was each administered, intratracheally, 5 ug of radiolabeled $BaSO_4$. Five rats were killed after 24 hours and seven after seven days for tracheal examination. At 24 hours after administration, some of the $BaSO_4$ was still above the epithelium, but most of it had moved into the tracheal wall. While a small proportion of the $BaSO_4$ was found more than 50 um from the surface, there was a clear peak of retained material at 10-15 um. The peak was 0-5 um beneath the basement membrane. By seven days, practically all of the retained $BaSO_4$ was beneath the epithelial surface (10).

- Particles of $^{133}BaSO_4$ were deposited on the surface of rat trachea by intratracheal injection. Aggregates of particles were located in the trachea by autoradiography and electron microscopy (EM). Following depositions, particles not rapidly removed by

3

muco-ciliary clearance remained on the epithelium for some time. After two hours most had been ingested by macrophages on the surface, though some were still free in the mucus. By 24 hours, 74% of the aggregates remaining were beneath the epithelium in the lamina propria, and after seven days almost all of them were in or beneath the epithelium. All the buried particles identified by EM were within macrophages. After 24 hours the particles in the tracheal wall were beneath epithelium which was not ciliated columnar, but cuboidal or flatter, with fewer or no ciliated cells and infiltrated with lymphocytes. It is suggested that particle retention in airways is accomplished by ingestion by macrophages which then migrate through this type of epithelium (20).

- Sixteen cases of aspiration of $BaSO_4$ were reviewed. None showed any signs of acute or chronic toxic effects (22).

- See Related References 27-35 for additional information.

5. Intravenous Injection

   - Respiratory resistance was measured by a forced oscillation technique in vagotomized guinea pigs before and after micro-embolism produced by i.v. injection of 0.5 mL/kg of 10% $BaSO_4$. Micro-embolic challenge with $BaSO_4$ increased respiratory resistance by 27%. No change in respiratory compliance or arterial platelet numbers were observed following low dose $BaSO_4$ micro-embolism. This suggests that pulmonary micro-embolism produced a decrease in medium or large airway calibre (6).

6. Intramuscular Injection

   - Radiolabeled barium sulfate was injected intramuscularly into one hind leg of each of five rats. At various times after injection to about one year, the rats were individually scanned for radioactive barium distribution. The sulfate showed a half-life of loss from the injection site of 26 days. Beyond about 100 days, the radioactive barium localized primarily in bone, where it resided with a biological half-life of 460 days (42).

B. Extended Studies

1. Oral

- Groups of mice were fed diets containing 0, 0.008, 0.08, 0.8, and 8 ppm $BaSO_4$ along with small amounts of Sc, Cr, La, Sm, Eu, Tb, Dy, Tm and Yb. The experiment ended when the young from the third generation adults were weaned. Mortality and morbidity were negligible. No consistent growth rate changes were observed. However, different groups showed different growth rates during different generations. The number of mice born showed no significant differences among treatment groups. Survival, growth rate, hematology, morphological development, maturation, reproduction and lactational performance were comparable to those mice fed the basal diet (16). A subsequent study in monkeys confirmed these results (14).

2. Inhalation

- The chronic inhalation of 250-300 mg/m^3 of $BaSO_4$ in rats produced granuloma formation, intramural bronchial and peribronchial infiltration and proliferative changes in the lungs (12).

- A group of rats was exposed to 40 mg/m^3 of $BaSO_4$ for two months. They were then observed for an additional four weeks. Animals were sacrificed at 14-day intervals and their lungs and lymph nodes histologically examined. An initial rapidly progressing cellular reaction of the lung parenchyma is followed by proliferation of alveolar macrophages and peculiar modification of bronchiolar epithelium. These epithelial changes regress slowly during the experiments without, however, causing lung damage. In the authors' opinion the changes justify the classification of $BaSO_4$ as an inert dust (9,13).

- A group of 32 rats was administered 20 mg of $BaSO_4$ intrapleurally. Following injection the rats were fed a standard diet and allowed to live until natural death. One rat in the 30 examined histologically had a mesothelioma. Occasional mesotheliomas were also produced by glass powder, Al_2O_3 and ceramic fiber (21).

- Groups of rats were administered 26 ug $BaSO_4$ intratracheally. Animals were serially sacrificed over a nine-month period. Pathological examination did not reveal any difference between the control and experimental animals (2).

- Groups of rats were administered 26 ug of either radiolabeled or inert $BaSO_4$ per week for ten weeks by the intratracheal route. The rats that had been exposed to the radioactive particles showed many types of severe pulmonary changes. Dilated bronchi filled with pus, atelectasis, emphysema, fibrosis, interstitial pneumonitis, bronchiectasis, edema, squamous metaplasia and squamous-cell carcinoma are among the pathology findings. One rat died from fibrosarcoma that had metastasized to the lungs and kidney. The group administered inert $BaSO_4$ showed very little pulmonary pathology. The main finding was mild murine pneumonia thought not to be compound-related (4).

- A group of twenty dogs was administered one to ten mL of $BaSO_4$ intratracheally. Animals were sacrificed at one, two, 24 and 48 hours and 12, 14, 17 and 168 days. Clinically, the dogs manifested no ill effects. Pathologically it was observed that when sufficient $BaSO_4$ remained in the bronchioles to become extended, focal atelectasis and emphysema resulted. Histologically, the retained $BaSO_4$ stimulated only a bland foreign body reaction (22).

C. Carcinogenic Potential

- No tumors were reported in three-generation feeding studies in mice and monkeys (14,15). Inhalation studies have not shown $BaSO_4$ to have carcinogenic potential (9,13,18). Intrapleural or intratracheal administration has also failed to show a carcinogenic potential for $BaSO_4$ (24,21). An intratracheal study with radiolabeled $BaSO_4$, proved it to be carcinogenic. This effect is due to the radioactivity and is not caused by $BaSO_4$ (4).

- Rats were implanted with polyethylene film and polyethylene devices. $BaSO_4$ was added as a radiopaque substance. One sample of film was implanted without any $BaSO_4$. $BaSO_4$ had no effect on the incidence of tumors at the implantation site (19).

D. Mutagenic Potential

No information available.

E. Embryotoxic Potential

No information available.

F. Other Reproduction Studies

- No effect on reproduction was seen in a three-generation feeding study in mice (15).

G. Aquatic/Environmental Studies

- $BaSO_4$ was not toxic to fish in concentrations up to 100,000 ppm in fresh or sea water (12).
- See Related References 36 and 37.

H. Clinical Reports of Human Exposure

- Inhalation of barium sulfate dust causes a pulmonary reaction with mobilization of polymorphonuclear leukocytes and macrophages and characteristic radiographic changes with dense, discrete small opacities distributed throughout the lung fields (baritosis). The shadows appear to be due to the radioopacity of $BaSO_4$ itself rather than to any tissue lesions, and the condition is symptom-less with no abnormality of pulmonary function (40,43).
- Barium enema examination using $BaSO_4$ as the radio-opaque agent has had a very low complication rate, approximately two in 10,000 cases. During a 20-year period at a major New York City hospital, only 18 examples were found of perforation of the colon during barium enema examination. Barium enemas have also been associated with peritonitis, appendicitis and granuloma of the rectum. As these clinical cases are outside the scope of this search they are mentioned only to indicate that there is literature available. A search of Toxline or Medline will result in a number of reports.

I. Epidemiology

No information available.

J. Metabolism

- Radiolabeled $BaSO_4$ was orally administered to rabbits. The radioactivity of feces, blood and urine were estimated. Fecal ash had the greatest radioactivity 18 hours after administration, blood ash on the second day and urine ash on the fourth day (17).

K. Biochemical Studies

- See Related Reference 39.

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September 27, 1978

Updated:
May 11, 1983:WP:3.3

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AR306673

March 12, 1991
Project No: 400754

APPENDIX E

Zinc

Patty's Industrial Hygiene and Toxicology

THIRD REVISED EDITION

Volume 2A
TOXICOLOGY

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39 ZINC, Zn

39.1 Source and Production (1, 2)

Zinc is widely distributed and occurs in small amounts in almost all igneous rocks. Sphalerite (zinc blende), ZnS, is the principal Zn mineral. Depending on Fe content, natural specimens range in color from light tan to black; above a ratio of Fe:Zn of 1:5 the mineral is called marmatite; above 5:6 the sphalerite structure ceases to exist. Next to Fe, Cd is the most common impurity in sphalerite; when associated with Zn as CdS it is called greenockite. Cadmium is about 1/200 as abundant as Zn. Gallium and Ge also occur in sphalerite (low temperature formation); Sn and In occur in traces from high temperature deposits. Lead minerals are commonly associated with Zn minerals; the Zn/Pb ratio varies widely, from 1:7 to 5:1. Other commonly associated minerals are calcite ($CaCO_3$), dolomite ($CaCO_3 \cdot MgCO_3$), pyrite (FeS_2), quartz (SiO_2), chalcopyrite ($CuFeS_2$), and barite ($BaSO_4$). Other oxidized forms of Zn minerals, such as ZnO, $ZnSO_4 \cdot 7H_2O$, $ZnCO_3$, $Zn_4Si_2O_7(OH)_2 \cdot H_2O$, and $(Zn,Mn)O \cdot Fe_2O_3$, can be thought of as alterations from the sulfide, and are of minor importance.

Total U.S. mine production in 1975 was 469,355 short tons, 19 states contributing to the total. The major producing states were Tennessee, 18 percent, New York and Missouri, 16 percent each, Colorado, 10 percent, and Idaho, 9 percent. States east of the

Mississippi River accounted for about half the total mine production. Zinc recovery from secondary sources amounted to somewhat more than 225,000 tons; imports of ores and slab Zn amounted to approximately 525,000 tons. With export of slab Zn of about 7000 tons, the total tonnage for U.S. consumption in 1975 was approximately 1,232,000 short tons.

World mine production totaled 6,131,000 tons, originating from 54 countries worldwide. The seven leading sources were Canada, with approximately 1,194,000 short tons, followed by, with decreasing amounts, the Soviet Union, Australia, the United States, Peru, Japan, and Mexico, the last with 252,000 tons. The other 47 countries had considerably less than 100,000 tons each, with the exception of Poland, West Germany, Greenland, Sweden, Yugoslavia, China, and North Korea.

World smelter Zn production was confined to 32 countries worldwide and totaled almost 5,500,000 tons. The nine leading sources were Japan with 773,600 tons, followed by, with decreasing amounts, the Soviet Union, Canada, the United States, Belgium, Poland, France, West Germany, and Australia, with the remaining 23 countries smelting less than 100,000 tons each, with the exception of Mexico, Finland, Italy, Netherlands, Spain, Yugoslavia, China, and North Korea.

A variety of mining methods are used, which vary with the type of ore body. Underground methods account for most of the production but some open-pit mining is done. Almost all loading and transportation are handled by power, at present; electric or diesel units supply the power. Production of Zn concentrates is done by crushing and grinding followed by gravity separation, flotation, or magnetic methods, or combinations of them, depending on the complexity of the ore. Considerable metal loss occurs on concentrating; losses of 8 to 20 percent occur with the sulfide and 15 to 90 percent of the oxidized Zn. To improve recoveries of the latter, a caustic-leach electrolytic process is used; in this, Zn is extracted from the ores by NaOH solution, the resulting electrolyte is purified with Zn dust and lime, and the Zn is electrodeposited. Zinc smelting refers to treatment whereby Zn ores or concentrates are reduced to refined metal. Sulfide Zn concentrates are roasted to eliminate S; in the process Zn is converted to the oxide and small amounts of $ZnSO_4$. The roast may either be leached for electrolytic deposition of Zn or combined with coke or coal and retorted at about 1100°C. Residues from leaching and distillation are shipped to a lead smelter for further processing if they contain economic amounts of metals (Pb, Au, and Ag).

Electrolytically refined Zn is fast replacing smelter Zn not only in the United States but in other countries as well. Electrolytic Zn produced in the United States in 1975 amounted to slightly more than 232,000 tons compared with distilled Zn of about 206,000 tons. Redistilled secondary Zn from primary smelters was 15 percent, and from secondary smelters, 9.5 percent, respectively, for electrolytic Zn.

Domestic smelters produce Zn of various grades; electrolytic plants produce special high grade Zn or high grade slab Zn; slab Zn from horizontal retort plants is mostly prime western grade, although smaller amounts of other grades are produced; vertical retort plants produce regular high grade; all other grades are produced as the market warrants.

39.2 Uses and Industrial Exposures

Of the total U.S. domestic consumption of Zn in 1975, slab Zn comprised the major amount, 925,330 tons or 75 percent; Zn used for galvanizing was about 377,000 tons or 41 percent; Zn-base alloys, 334,200 tons; brass products, 115,300 tons; Zn oxide from slab Zn, 39,000 tons; rolled Zn, 27,300; and others, 32,600 tons.

A breakdown of consumption into nine major market categories, based on 1974 data, show that automotive components accounted for 51.2 percent; builder's hardware, 19.1 percent; domestic appliances, 8.5 percent; industrial, agricultural, and commercial machinery, 7.7 percent; electric components, 5.7 percent; sporting goods and toys, 2.8 percent; scientific and professional equipment, 1.6 percent; sound and television equipment, 1.2 percent; and miscellaneous, 2.2 percent.

Total use of Zn oxide in 1975 was about 180,000 tons, the major portion of which, 57 percent, went to the rubber industry as a pigment and as an aid in vulcanizing. Photocopying used 15 percent, chemicals 10 percent, and paints, 6 percent. ZnO was also used in floor coverings, fabrics, lubricants, plastics, and rayon manufacture. The chief use of Zn sulfate was in agriculture with lesser amounts for rayon, flotation agents, and chemicals. Leaded ZnO was used in rubber, and Zn chloride, in soldering fluxes and batteries.

Industrial hazards arise from exposure to Zn fume, a notorious producer of metal fume fever, but associated hazards in the metallurgy of Zn, of more serious consequence, arise from the presence of As, Cd, Mn, Pb, and possibly Cu and Ag. The frequent presence of As in Zn is a source of exposure to arsine (AsH_3) whenever Zn is dissolved in acids or alkalies; many cases of intoxication by AsH_3 have occurred in the pickling of galvanized iron or from the use of powdered impure Zn as a reducing agent in dyeing. It is possible also that effects attributed to exposure to Zn fume may in part be attributable to those of Cd. Cadmium occurring uniformly as a contaminant in Zn is a continuous source of trace amounts of Cd in man.

39.3 Physical and Chemical Properties

The physical and chemical properties of Zn and some of its more important industrial compounds are listed in Table 29.39.1.

Zinc is a silvery metal of low to intermediate hardness; rolled Zn, 99.94 percent purity, has a scleroscope hardness of 13 to 15; cast Zn of the same purity is slightly softer. The effect of small amounts of common impurities is to increase corrosion resistance to solutions, but not in the atmosphere. Ordinary Zn is too brittle to roll at ordinary temperatures, but becomes ductile at elevated temperatures; brittleness is thought to be associated with impurities such as Sn.

Zinc has a standard electrode potential of +0.761 and is thus electropositive to most structural metals except Al and Mg. This property is the basis of many important uses of Zn, for example, in batteries and electrogalvanizing of steel. Zinc is attacked by moist air, CO_2, and SO_2, resulting chiefly in a coating of hydrated basic carbonate of variable

Table 29.39.1. Physical and Chemical Properties of Zinc and Some of Its Compounds

Form of Zn	At. or Mol. Wt.	Sp. Gr.	M.P. (°C)	B.P. (°C)	Solubility
Zinc (Zn)	65.38	7.14	419.58	907	Insol. hot or cold H_2O; sol. acids, alkalies, acetic acid
Zinc oxide (zincite) (ZnO)	81.37	5.606	1975	—	1.6 mg/liter (29°C); sol. acids, dil. acetic acid, insol. NH_4OH, alcohol
Zinc acetate $[Zn(C_2H_3O_2)_2]$	183.46	1.84	Dec. 200	Subl. vac.	300 g/liter (20°C), 146 g/liter (100°C); 28 g/liter alcohol
Zinc chloride ($ZnCl_2$)	136.28	2.91 (25°C)	283	732	4.32 kg/liter (25°C), 6.15 kg/liter (100°C); 1 kg/liter alcohol (12.5°C); v. sol. ether; insol. NH_3
Zinc cyanide $[Zn(CN)_2]$	117.41	1.852	Dec. 800	—	5 mg/liter (20°C); sol. alkali, KCN, NH_3; insol. alcohol
Zinc fluoride (ZnF_2)	103.37	4.95 (25°C)	872	Ca. 1500	16.2 g/liter (20°C); sol. hot acid, NH_4OH; insol. alchohol
Zinc nitrate hexahydrate $[Zn(NO_3)_2 \cdot 6H_2O]$	297.47	2.065 (14°C)	36.4	$-6H_2O$, 105–131	1.843 kg/liter (20°C), inf. sol. hot H_2O; v. sol. alcohol
Zinc stearate $[Zn(C_{18}H_{36}O_2)_2]$	633.33	—	130	—	Insol. cold H_2O; insol. alcohol, ether
Zinc sulfate (zincosite) ($ZnSO_4$)	161.43	3.54 (25°C)	Dec. 600	—	865 g/liter (80°C), 808 g/liter (100°C), sl. sol. alcohol
Zinc sulfide, β (sphalerite) (ZnS)	97.43	4.102 25°C)	Tr. 1020	—	0.65 mg/liter (18°C); v. sol. acids

composition; some H_2O_2 may be formed in the process. Zinc is resistant to attack by dry F_2, Cl_2, and Br_2 but combines rapidly in presence of water vapor. Zinc is attacked by acid gases and acids. Zn is an active reducing agent for many ions such as Fe^{3+}, MnO_4^-, and CrO_4^-. Hot caustic solutions form zincates of uncertain composition. Zinc vapor reduces CO_2 to CO, the amount depending on the temperature; above 1100°C, the retort temperature of Zn distillation, essentially all CO_2 is reduced to CO, in the presence of excess C. Zinc and S will explode when mixed as a powder and warmed. A protective coating of ZnS is formed on masses of Zn by either S or H_2S. When Zn or one of its alloys is burned, melted, or heated to temperatures above 930°F, Zn metal metal oxide fume of particle diameter 1 μ and below is formed.

Zinc alloys are numerous, and most have been in use and standardized for several decades. If Zn is the primary constituent of the alloy, it is a Zn-base alloy. Zinc also is commonly used in varying degrees as an alloying component with other base metals, such as Cu, Al, and Mg. A familiar example of the latter is the association of varying amounts of Zn (up to 45 percent) with Cu to produce brass, the third largest use of Zn in the United States.

Zinc-base alloys have two major uses, for casting and for wrought applications. Casting includes both die-casting, which is the largest single market for Zn in the United States and second largest on a world basis, and gravity-casting, which differs from die-casting primarily in that no pressure is applied, except the force of gravity, in forcing the molten metal into the mold.

In the case of wrought Zn, numerous compositions and alloys are used, depending on ultimate product requirements. Alloying metals can be used to improve various properties, such as stiffness, for special applications. The Zn–Cu–Ti alloy has become the dominant wrought-Zn alloy for applications demanding superior performance. Composition of this alloy is 0.4 to 0.8 percent Cu, 0.08 to 0.16 percent Ti, 0.3 percent max. Pb, 0.015 percent max. Fe, 0.01 percent max. Mn, 0.01 percent max. Cd, 0.02 percent max. Cr, and the balance, special high grade Zn.

The properties of Zn–Cu–Ti wrought-Zn alloy that make it useful are greater strength and dent resistance than other metals of the same thickness. It is easily soldered, is nonmagnetic, and has an electric conductivity equal to that of brass.

Of all the structural metals, Zn has more products and compounds commercially available than any other at the present time; more than 70 Zn substances are presently listed in the *Chemical Buyers Directory* (723), 34 of which are organic derivatives.

Of all the compounds Zn oxide leads the others in total use (180,000 tons) because of its numerous applications in both heavy and light industry. In heavy industry its main use is as an accelerator–activator, pigment, and reinforcer in rubber and high polymers; as pigment and mold-growth inhibitor in paints; in light industry, in cosmetics and ointments; as semiconductor in electronic devices; as photoconductor in office copying machines and in color photography; and as a feed additive.

Apart from sharing the common property of color, all Zn compounds being white (with the exception of those with a chromophore group like $ZnCrO_4$), the anionic groupings confer on each Zn compound special properties leading to special uses. For

example, of the two Zn halides, Zn chloride and fluoride, although both share in catalytic behavior and in wood preservation, the main use of the chloride is in soldering and welding fluxes, whereas the fluoride is a termite repellent. Zinc acetate, also a wood preservative, because of its high solubility in water, is used as a mordant in dyeing, and a cross-linking agent in polymerization. In like manner, Zn cyanide, because of its property of liberating cyanide in dilute mineral acids, finds use as an insecticide and in metal plating. The nitrate finds use as a catalyst, a latex coagulant, and a mordant, while the special property of oiliness of Zn stearate makes it useful as a lubricant and as a mold-release agent in the rubber industry, and in cosmetics. The greatest use of Zn sulfide is in making lithopone pigment (28 percent ZnS and 72 percent $BaSo_4$) which is used in paint, linoleum, and artificial leather, in addition to many other uses such as a phosphor in X-ray and television screens, and in luminous watch faces. Zn sulfate has varied uses also from a preservative for skins and wood, to bleaching paper (with hypochlorite), to feed and soil additive and fungicide.

39.4 Analytic Determination

Before the advent of atomic absorption spectrometry (AAS), the determination of Zn was made by colorimetry, using dithizone of di-β-naphthylthiocarbazone, or by polarography after collection by means of an impinger, electrostatic precipitator, or molecular membrane filter (1631). Because of greater speed and equal accuracy, AAS is the method of choice for its determination in air, urine, and other biologic samples (1632), and is recommended for determining Zn oxide fume and dust in air by the Analytic Branch of NIOSH (Method 222, Vol. I, 2nd ed., 1977) (686). Cellulose membrane filters of pore size 0.8 μm are recommended for sampling freshly formed oxide. The optimal working range is from 0.025 to 2 μg Zn/ml, and the sensitivity is 0.025 μg Zn/ml. No interferences have been found. Because there is no sample preparation, the method is rapid; however, because AAS measures total Zn, differentiation of various Zn compounds cannot be made.

For those who cannot employ AAS, an improved colorimetric procedure for the determination of serum Zn has been reported (1633). Following a guanidine HCl addition to release Zn from protein, and complexing of the release metals with cyanide, the complex is "demasked" with chloral hydrate, and reacted with the colorimetric reagent 4-(2-pyridylazo)resorcinol. The complex has an absorption maximum at 497 nm. The values found by this method were reported to compare favorably with those from AAS.

39.5 Physiologic Response

A brief review of Vallee (6 pages, 28 references) touching on many of the salient features of Zn and its biologic significance to man appeared in 1957 (1634). Sufficient evidence has accumulated to show that Zn occurs in the body in two different protein combinations: (1) as a metalloenzyme in which Zn is an integral part of an important enzyme

system, such as carbonic anhydrase for the regulation of CO_2 exchange, and (2) as a metal–protein complex in which Zn is loosely bound to a protein, which acts as its carrier and transport mechanism in the body (metallothionein).

Since that time, the biologic literature on Zn has overflowed with the role of Zn in (1) several important enzyme systems, RNA polymerase, superoxide dismutase, carboxypeptidase, isocitric dehydrogenase, alcohol dehydrogenase, and others, (2) food nutrition, and (3) Zn deficiency states, about which literally hundreds of articles have appeared annually since 1975; some relate to diseases of the skin. (See *Index Medicus,* 1975 and later.) The possible relation of these Zn–protein combinations in altered metabolic conditions and diseases is pointed out, and is discussed in more detail here in the appropriate sections.

39.5.1 Acute Toxicity

Zinc salts of strong mineral acids are astringent, corrosive to the skin, and irritating to the gastrointestinal tract; when ingested, they act as emetics. Zinc 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 gastroenteric mucous membranes. Mass poisonings have been repeatedly recorded (1635) from drinking acidic beverages made in galvanized containers; fever, nausea, vomiting, stomach cramps, and diarrhea occurred in 3 to 12 hr following ingestion. The emetic concentration range in water is from 675 to 2280 ppm; the threshold concentration of taste for Zn salts approximates 15 ppm; 30 ppm soluble Zn salts imparts a milky appearance to water, and 40 ppm, a metallic taste (1636).

Aside from their irritant action, inorganic Zn compounds are relatively nontoxic by mouth (171). Acute oral toxicity in laboratory animals ranges from 250 mg/kg for lowest lethal dose (LD_{LO}) for ZnF_2 for the guinea pig to 1190 mg/kg as rat oral LD_{50} for Zn nitrate hexahydrate, and 2200 mg/kg for the rat oral LD_{LO} for $ZnSO_4 \cdot 7H_2O$, to 2460 mg/kg for Zn acetate dihydrate. By parenteral routes, however, inorganic Zn salts are highly toxic; the intravenous LD_{50} and LD_{LO} for $ZnSO_4$ and its heptahydrate are, respectively, 40 and 49 mg/kg, and the LD_{LO} for $ZnCl_2$ by the same route for the rat is very similar, 30 mg/kg. Oddly, the rat intraperitoneal LD_{LO} for the cyanide is greater, 100 mg/kg.

The acute toxicity by the subcutaneous route appears to be intermediate between intravenous and oral routes; the rat subcutaneous LD_{LO} for $ZnSO_4 \cdot 7H_2O$ is 330 mg/kg, and that for ZnF_2 for the guinea pig, 100 mg/kg. Strangely, no experimental acute toxicity data could be found on ZnO, the compound presenting the greatest industrial exposure.

Many unsuccessful attempts have been made to reproduce in animals Zn metal fume fever, the chief occupational toxicity problem associated with exposure to Zn. Pernis et al. (1637), after having reviewed reports and their hypotheses, showed that preliminary exposure to acetic acid vapors tended to prepare the host for the development of Zn

metal fume fever by permitting contact between leukocytes and ZnO particles, resulting in the release of endogenous pyrogens leading to metal fume fever. For Zn fume fever in the industrial setting, see Section 39.5.6.

The acute toxicity of organic derivatives of Zn would appear, based on limited data (171), to resemble that of the inorganic compounds for the most part; for the agricultural chemical Ziram (dimethyl dithiocarbamate), whose rat oral LD_{50} is 1400 mg/kg, the intraperitoneal LD_{50} is 23 mg/kg. Data are lacking to show whether this relation holds for other organic derivatives such as Zineb, Zn ethylenebis(dithiocarbamate), Zn naphthenate, or Zn acetylacetonate, although on present evidence it would appear so.

The single piece of acute toxicity data for man relates to the inhalation of $ZnCl_2$ dust; a 30-min exposure at 4800 mg/m^3 constituted the lowest toxic concentration, TC_{LO}. When this is parenterally administered, Zn depresses the central nervous system, causing tremors and paralysis in the extremities.

39.5.2 Chronic Toxicity

To emphasize the low oral toxicity of Zn compounds it is only necessary to refer to Drinker et al. (1639); these investigators gave 175 to 1000 mg of ZnO/day for periods of 3 to 53 weeks to dogs and cats, and it was tolerated; glycosuria occurred in the dogs, and fibrous degeneration of the pancreas in some of the cats was found at autopsy. No manifest injury occurred in rats from administration of 0.5 to 34.4 mg ZnO/day for periods of 1 month to 1 year. Similar lack of response from $ZnCO_3$ is reported. On the other hand, Waltner and Waltner (1640) reported that feeding the same salt induced anemia and osteoporosis in rats; 2 percent metallic Zn in the diet of rats, however, resulted in no injury. Zinc acetate fed to rats for 4 months in doses of 10 to 15 mg daily and 50 mg of Zn malate fed to cats for 10 days to 2 months caused no intoxication, according to Salant (1641). Sutton and Nelson (1642) found that 0.1 percent Zn was tolerated in the diet of rats, but that more than 0.5 percent reduced their capacity to reproduce, and 1 percent inhibited growth and caused severe anemia and death. Zinc salts in the diet are somewhat more toxic to pigs (1643).

Severe anemia of the hypochromic, microcytic type has resulted in 3 to 5 weeks in animals on a dietary level of 1.0 percent Zn as lactate, as well as limiting growth and reproduction (1644).

The experimental production of Zn fume fever in brass foundry workers, its clinical description, and conditions under which it occurs have been reported in a series of five reports by Drinker and associates (1645). Brief exposures of 5 to 12 min to Zn oxide fume of two workers, who had experienced metal fume fever (MFF) on several occasions during the preceding 2 years, at concentrations that would be considered today as impermissibly high (up to 600 mg/m^3 as Zn) resulted in typical metal fume fever. (For description, see Section 39.5.5.) Symptoms appeared in about 7 hr in the first worker and in 4 hr in the second worker, who had breathed the fumes for 12 min (1645a).

When these exposures were repeated in a brass foundry at somewhat lower, but still high concentrations (ca. 330 mg Zn/m^3), some workers acquired resistance, developed after the third daily exposure of a few hours each, that either attenuated or prevented the prodromal symptoms altogether (1645b).

In the third report (1645c) Zn fume fever was shown to develop after exposure to Zn oxide powder, freshly prepared, and very fine (ca. 0.15 μm in particle diameter).

In the fourth report (1645d) it was shown that for the Zn fume to develop the characteristic symptoms, slow, deep, breathing at levels greater than 15 mg/m^3 was required (1645e).

Teratology. The agricultural chemicals Zineb [Zn ethylenebis(dithiocarbamate)] and Ziram (Zn dimethyl dithiocarbamate), when tested for teratogenic effects orally in rats proved to retard onset of pregnancy and produce infertility, resorption of fetuses, or developmental anomalies in offspring in 2 to 4 months on daily doses of 100 and 50 mg/kg, respectively (1646a). Both chemicals in doses of 10 mg/kg caused only slight changes in reproductive function in a few of the test animals, and were without effect on the offspring.

Zineb and Ziram were found not to be mutagenic when tested on drosophila strain Clb, and the morphogenic changes in drosophila caused by Zineb agreed with the findings obtained in the rats. Additionally, developmental anomalies were not found in the offspring of second-generation rats, so that no new mutations had occurred.

Teratologic evaluation has also been made of Zn pyrithione [1-hydroxy-2-(1*H*)-pyridinethione], a broad spectrum antifungal and antimicrobial agent used in formulations coming in contact with the skin and in shampoos and hairdressings as an antidandruff agent (1646c). Because ≥2.5 percent is absorbed through the skin in various species, evaluation has been made in both pigs (1646c) and rabbits (1646b). In both studies, no evidence of any teratogenic or embryotoxic effect was observed in any of the fetuses or dams.

39.5.3 Metabolism

Zinc is omnipresent in living organisms and ranks with the most abundant of the trace metals in man. As far as is known, all living things require Zn, and it is a constituent of all cells serving as a cofactor in many essential enzyme systems. For this reason, Zn has been found in all specimens of all 29 tissues analyzed (1182).

Normal Values. For adult U.S. subjects of ages representative of industrial workers, the average Zn concentration of eight organs and tissues in μg/g ash in decreasing order were as follows: kidney, 4900 ± 140; liver, 3800 ± 110; heart, 2800 ± 67; pancreas, 2400 ± 70; aorta, 1900 ± 70; lung and spleen each, 1400 ± 35 and 29; and brain, 820 ± 34 (1647). Of all tissues, prostate had the highest Zn concentration, with values reaching 10,000 ppm in some specimens; muscle, both striated and nonstriated, had

about half that of the prostate. Sections of the gastrointestinal tract ranged from 1700 to 3500 ppm with no consistent order aborally. Some specimens of fat contained 2000 ppm Zn, but oddly, bone contained the least, 210 ± 5 ppm.

The only organs showing marked correlation with age was the prostate, in which Zn increased, and the uterus, in which it decreased. In the kidney, Zn increased from 4500 ppm at 20 to 29 years to 5500 at 40 to 49 years, after which it decreased to 4000 at age 80, paralleling Cd concentration changes. Other organs, liver and pancreas, tended to increase slightly after 40, whereas the Zn in lung, spleen, and brain remained relatively constant through life after 20 years of age. Heart and aorta tended to show a downward trend with age after 30 (1647).

Normal values of Zn in blood and urine are few; Vallee (1648) reported values in human serum of 109 to 130 μg Zn/100 ml, similar to those of Fe; whole blood Zn, 880 ± 200 μg/100 ml; and red cell Zn, 1440 ± 270 μg/100 ml. This value for whole blood is in fair agreement with the value of 580 μg Zn/100 ml obtained by mass spectrometry 15 years later (1364). Similarly, the value for urine estimated by Schroeder et al. (1647) of less than 500 μg/day and the value of 150 μg Zn/liter obtained by mass spectrometry are of the same order of magnitude.

Zinc values in hair as a factor in Zn metabolism (1649), determined in six young male adults in Rochester, New York in 1961, were found to have seasonal variation; marked elevation in Zn values of 20 to 90 percent, from a low normal of 100 ppm, occurred in the summer months from June to September. There was also a distinct sex variation; females tended to have a threefold greater concentration of hair Zn than males of the same age, whereas young offspring, 6 years and younger, had one-quarter to one-half as much as mother and father.

Sweat can represent a sizable route of Zn excretion, according to Prasad, et al. (1650); depending on climatic conditions, Zn loss in sweat can range from 1150 ± 300 μg Zn/liter in temperate climates to 2300 to 12,700 μg Zn in 2 to 11 liters/day in hot climates.

From the above values, a Zn balance in man has been estimated by Schroeder et al. (1647) to approximate the following:

Intake	mg Zn	Output	mg Zn
Food	12.0	Urine	0.5
Water (tap)	0.5	Feces	10.6
Air	0.1	Sweat	0.5
		Other (blood, semen)	1.0
Totals	12.6		12.6

It should be noted that variations in each of these estimates can be large; taking extreme examples of output of 2.0 mg via urine, 10 mg in sweat, and 1 mg in semen or blood loss, 13 mg in food would need to be absorbed to maintain balance. At the other extremes of 10 μg in urine, no sweating, and no loss of blood or semen, balance could be

maintained on very little Zn being absorbed, enough to account for losses in skin and hair. The amount absorbed from foods can be influenced by the presence of phytic acid, which makes bound Zn unavailable, and possibly by the intake of Ca, although this is uncertain in man.

Zinc in Disease States—Protective Effects. Zinc has been long known to exert protective effects in many disease states, essentially for two reasons: (1) Zn is a metal essential for the activity of several critical enzyme systems; and (2) Zn, as a divalent cation, can replace other similar cations that can lead to disease states (e.g., liver injury by Mn). The best known in industrial toxicology because it has been the most studied is the antagonism of Zn for Cd intoxication in the kidney; at a Zn/Cd ratio of 1:1 when toxicity is manifest, a Zn/Cd ratio of 4:1 prevented toxic manifestations (355) (see Section 7.5.5.3). Similarly, Zn has been shown to prevent the inhibitory effect of Pb on the red cell enzyme ALA dehydratase, presumably by inducing more synthesis of the enzyme for which Zn is an essential component (1651). [Closely related to this Zn–Pb interaction is the rise in red cell Zn protoporphyrin levels in Pb workers at low blood Pb levels (836a, b).]

Zinc has shown protective effects in several other conditions, some of which follow. Sickle cell anemia, of which there is an estimated frequency in blacks of 5 percent, and in some of whom there is a Zn deficiency, responds well to Zn treatment (1652), thus being an unusual instance in which an industrial exposure can exert a beneficial effect.

In another condition of Zn deficiency, acrodermatitis enteropathica, an inherited, autosomal, recessive disorder of Zn metabolism, restoration to normal plasma Zn levels by ionic Zn administration corrected the condition by correcting a defective chemotaxis of the neutrophils and monocytes (1653).

The capacity of Zn to accelerate wound healing is well documented (1654), and on the basis, oral $ZnSO_4$ reduced joint swelling, morning stiffness, improved walking time, and overall general condition in 24 patients with chronic, refractory rheumatoid arthritis (1655). The rationale for its efficacy is that local synovial Zn levels are depleted.

In a reverse manner, Zn deficiency proved to retard the growth of Walker 256 carcinosarcoma in rats, indicating a Zn requirement for the growth of this tumor (1656).

Absorption, Distribution, Excretion. Only very small amounts of Zn are absorbed and stored in the tissues of laboratory animals, dogs, cats, and rats fed Zn compounds for long periods (1639); chief sites of storage were the liver and pancreas. Intravenously injected radioactive ^{65}Zn, however, showed that liver, pancreas, and kidney stored large amounts of ^{65}Zn, and that the muscular and mucosal layers of the small intestine contained relatively large amounts; more than 50 percent of the dose was excreted by mice in the feces and 2 percent in the urine in 170 hr (1657).

In man, on an average daily intake of 10 to 15 mg Zn, most is excreted through the intestines. The largest storage depot of Zn is striated muscle, where 62.6 percent of the

total is found. Bone contains 20.1 percent, liver 3.4 percent, blood 2.1 percent, the gastrointestinal tract 1.7 percent, and skin 1.6 percent of bodily Zn. Smooth and cardiac muscle combined (heart, bladder, gastrointestinal tract, uterus) contained 2.3 percent. No other trace element known is stored in muscle to this extent. The concentration of Zn is higher than that of Ca in muscle, is half that of Ca in heart muscle, and two-thirds that of Ca in liver. Therefore, Zn ranks with one of the bulk elements in these tissues (1647).

In young women taking a combination of oral contraceptives (+OCA), and in women with normal menstrual cycles (COCA), Zn excretion under negligible Zn intake (0.17 mg/day) showed a decline in serum Zn of 47 percent in the +OCA group and 21 percent in the −OCA group, and a corresponding decline in urinary Zn of 83 and 62 percent, respectively (1658). These data suggest that accessible stores of Zn are not extensive, and that depletion of these stores, as a result of the low-Zn diet, caused a fall in serum Zn. Chronic Zn deficiency on a dietary basis has been reported in male Iranian and Egyptian subjects showed dwarfism, hypogonadism, hepatosplenomegaly, and geophagia. The syndrome resembled experimental Zn deficiency in animals, and was associated with depressed levels of Zn in plasma, red blood cells, hair, and sweat (1650).

EDTA administered intraperitoneally to rats greatly increased urinary excretion of Zn (1659).

39.5.4 Mechanism

As noted above, Zn is an essential component of numerous enzyme systems of diverse activities, and thus enters into so many and varied biochemical and toxicologic reactions that it is possible to present only some of the more recent findings of how Zn behaves in the body that were not known at the time of the second edition.

The high complexing capacity of ionic Zn which permits it to interchange from one protein site to another, during metabolic activity, is the basis governing its action in the body. Evidence for the transfer of Zn from one protein to another is furnished by the binding of penicillamine, promoting gastrointestinal absorption of Zn (1660), histidine, EDTA, and aspirin to a Zn–protein complex in the intestinal content, intestinal mucosa, and blood plasma (1661). Amino acids, particularly histidine, are involved in the passage of Zn from the intestinal lumen to the bloodstream, and EDTA was found to bind Zn in the intestinal digesta; it remained bound as it passed through the intestinal mucosa, and was transported into the blood plasma. Similarly, aspirin is bound to the same protein in the mucosal soluble fraction that carried Zn.

The known anti-inflammatory properties of Zn ion can now be explained: the stabilization of lysosomal membranes (1662), the inhibition of prostaglandin synthesis (1663), interference with the complement system (1664), and impairment of macrophage function (1665).

In normal vitamin A metabolism, liver vitamin A stores are mobilized to the plasma. This is altered in Zn deficiency; vitamin A is not released from the liver. This is due to

a significant depression of plasma and liver retinol-binding protein (RBP) as a result of a depressed synthesis of liver RBP. The postulated mechanism is that the primary effect of Zn on vitamin A metabolism occurs through retinene reductase, believed to be a Zn metalloenzyme. This enzyme is an alcohol dehydrogenase, necessary for the conversion of vitamin A alcohol (retinol) to vitamin A aldehyde (retinene), a process essential for normal vision (1666).

Because proper evaluation of the toxicity of industrial chemicals often depends on controlled dietary intake of protective nutrients like Zn, Murthy and Petering (1667) varied dietary Zn (and Cu) levels in rats, and found that high levels of Zn produced anemia by inversely affecting hemoglobin and hematocrit levels. Also, although serum glutamic oxaloacetate transaminase (SGOT) values increased significantly from 170 to 204 m units/ml serum when Zn in the drinking water increased from 2.5 to 10 μg/ml, they declined thereafter to below-normal values when Zn levels were increased to 40 μg/ml, all of which shows that disregard for levels of dietary metal supplements can lead to erroneous interpretations of toxicity data.

Serum Zn level is lowered in experimental CS_2 poisoning (1668), pneumonia, bronchitis, erysipelas, pyelonephritis, and untreated pernicious anemia (1634). The mechanism for the lowered serum Zn levels in CS_2 poisoning is known; Zn complexes with the compound formed with CS_2 and the end amino acids of protein and is thus excreted (1668).

39.5.5 Industrial Experience and Epidemiology

Of the several effects resulting from industrial exposure to Zn, that of Zn fume fever (ZnFF) from freshly formed ZnO fume takes center stage attention for being most commonly described and best documented.

Lung Effects. In a survey of 102 brass foundry workers by Turner and Thompson (1669) 26 percent had attacks of "brass foundryman's ague" on the average of once a week, 13 percent once a month, 17 percent once a year, 11 percent twice a week, 14 percent twice a month, 6 percent twice a year, 2 percent three times a month, 1 percent three times a year, and 10 percent about four times a year. The attacks among 88 percent of the workers occurred only during winter months when ventilation was inadequate, but 12 percent had attacks regardless of season. Unfortunately, no environmental sampling was done, so it was not possible from this survey to arrive at a Zn oxide level that caused the attacks. Another syndrome, similar to brass foundrymen's ague, occurred in workers making Zn oxide powder; four of eight workers engaged in the bagging of freshly formed and still warm oxide powder had "oxide chills" and seven of nine in the packing room had similar symptoms.

Characteristic of the signs and symptoms of metal fume fever are the following. From 4 to 12 hr after exposure to freshly formed fumes, the worker begins first to notice an unusual metallic taste, or some alteration of familiar tastes, such as tobacco smoke. This is accompanied by dryness and irritation of the throat, with coughing and dyspnea, feel-

ings of weakness and fatigue, pains in the muscles and joints, and general malaise, similar to the prodromal syndrome of influenza. Fever then develops, associated with alternating chills. Body temperature is usually around 102°F, but may reach 104°F, with febrile shivering or rigors, accounting for the trade terms of "brass founders ague," "brass chills," "spelter shakes," and "Zn chills." The subject sweats profusely while the body temperature begins to fall, occasionally associated with convulsions. Severe pain in the chest, aggravated by difficult breathing, has been described by Fishburn and Zenz (1670). Clinical and symptomatic recovery usually is complete in 24 to 48 hr.

Clinical tests made during the acute phase show a polymorphonuclear leukocytosis, with the white count rising to 20,000 cells/mm^3; transient elevation in the lactic acid dehydrogenase isozyme factor 3 of the pulmonary parenchyma, in association with pneumonitis, was felt to be of value in a differential diagnoses of acute pulmonary symptoms (1670). Anseline similarly noted an elevation of pulmonary LDH isozyme in another case (1671).

Rapid development of tolerance is another characteristic feature of ZnFF, but it is lost as quickly; a Zn or brass worker may experience ZnFF on his first day back at work rather than during subsequent consecutive days of exposure. The acquired tolerance, believed to be an immunity (1672), is short-lived, and reexposure even on consecutive days may lead to repeated attacks of ZnFF.

The presumed mechanism of ZnFF development is given in Section 39.5.1 and Reference (1637).

The relation between the degree of exposure and the production of ZnFF was derived from the experimental human exposures by Drinker and associates (1645d), studies of Zn smelter workers by Batchelor et al. (1645e), and the work of Hammond (1673), who determined the incidence of ZnFF in pourers of molten Zn in the repair of stone crushers. At airborne levels of 8 to 12 mg/m^3 Zn oxide fume, no cases of ZnFF occurred. At airborne levels of 400 to 870 mg/m^3 Zn oxide and duration of exposure of 1 to 3 hr, all the workers experienced ZnFF at one time or another. Although the fume contained besides the Zn the alloying metals Mn, to the extent of 12.4 mg/m^3, and Pb, 1.6 mg/m^3, the great preponderance of Zn compared to Mn undoubtedly was responsible for the fever; Pb oxide fume is not an agent of fever.

Mogilevskaya, without reporting environmental levels, reported inflammation of the upper respiratory tract (nasopharyngitis, laryngitis) in 13 of 19 workers after 2 to 3 years employment in a Zn powder factory (1674).

Extensive fibrosis of the lung, ending in death, of a worker who had been exposed for 29 years to Zn stearate in a rubber factory was reported from Italy (1675). The exposures, unstated, must have been extremely high, because in the long years of exposure of workers to Zn stearate in a large U.S. rubber company, no adverse effects of any kind were experienced (1676).

Gastrointestinal Effects. Gastrointestinal disturbances have been reported in workers after prolonged exposures to ZnO, often mixed with NH_3, NH_4Cl, mineral acids, As, Sb, or Pb, for example. Later questions surrounding the validity of the claims

probably overlooked the fact that at the time of these reported complaints (1926–1936), exposure levels were considerably higher than in later years. Credence is gained by noting that the reports below emanated from the United States, Germany, Egypt, and Poland.

Gastrointestinal disturbances consisting of pressure in the stomach region, nausea, and weakness, which were suggestive of gastric or duodenal ulcers and which responded to an ulcer regimen, have occurred in workers employed for years in galvanizing (1677a), in torch-cutting of galvanized metal parts (1677b), in welding galvanized iron sheets (1677c), and in brass foundry work (1677d).

Clinically latent liver dysfunction has been reported in 15 of 25 workers exposed at high levels of Zn oxide (50 mg Zn/m^3) (1678) as evidenced by abnormal levels in liver function tests (alanine transferase, cholinesterase). Radiological evidence of peptic ulcer, found in three elevated uropepsin levels, was felt to be indicative of toxic damage to the gastrointestinal tract.

Effects on the Skin. Although ZnO is a constituent of many topical dermatologic preparations and has demonstrated low potential for skin irritation, nevertheless it was reported in 1921 (1674) that 14 of 17 men employed in making ZnO had experienced an occupational dermatitis, "oxide pox." The eruptions, which were small, red, hard, projecting papules with a white central plug, usually persisted for a week or 10 days. In 13 of the cases the pubic region, scrotum, and inner aspects of the thighs were involved, and in four cases, the axilla and inner surfaces of the arms as well. The author concluded that ZnO had combined with debris and bacteria to block sebaceous glands as a result of lack of personal hygiene.

39.6 Hygienic Standards of Exposure

The ACGIH has adopted TLVs for four Zn substances: Zn oxide fume, Zn oxide dust, $ZnCl_2$ fume, and Zn stearate. In the early 1950s the TLV for Zn oxide fume was set at 15 mg/m^3, the limit at that time for an "inert" particulate. This was later revised downward to 5 mg/m^3 in 1962 (see documentation of TLVs for 1974) (844). The latter is the permissible limit later adopted by most industrialized countries.

The TLV for $ZnCl_2$ fume, adopted in 1966, is 1 mg/m^3; for Zn stearate and Zn oxide dust, the TLV is 10 mg/m^3 or 30 mppcf, the limit for "nuisance" particulates.

OSHA adopted the TLVs for Zn oxide and Zn chloride fume in 1968.

The Soviet Union has an MAK for Zineb of 0.5 mg/m^3.

39.7 Flammability

Powdered Zn presents a hazard of explosion. If it is stored in damp places, there is danger of spontaneous combustion. Residues from reduction reactions may start a fire if thrown into combustible waste.

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40 ZIRCONIUM, Zr

40.1 Source and Production (1, 2)

Zirconium is associated with other metals in many minerals, but is recovered only from zircon ($ZrO_2 \cdot SiO_2$) and baddeleyite (brazilite) (ZrO_2). Hafnium, Hf, is invariably associated with Zr. Zircon occurs in all igneous rocks but is more common in granite, sylnite (complex silicates), and diorite (alkaline earth silicates). Zircon is a common constituent of river gravels and beach sands, whence it is recovered as a coproduct of ilmenite ($FeO \cdot TiO_2$), rutile (TiO_2), and monazite (Th and lanthanon phosphates). Baddeleyite usually occurs in phenolite and is also found in river gravels and beach sands; commercial deposits are known only in Brazil and the Republic of South Africa, but it is also found in East Africa, Sri Lanka, and the Soviet Union. Zircon sand is produced in Australia, Republic of China, Korea, and South Africa, India, and Brazil.

U.S. domestic zircon mineral production, mainly from Florida and Georgia, is estimated to be about 135,000 short tons annually, which is recovered from mineral sands by dredging and mining. Zirconium oxide production amounted to almost 12,000 tons in 1975.

World production of Zr concentrates, excluding that of the United States, which withheld production figures, amounted to 452,500 tons, 93 percent of which came from Australia, representing more than a fourfold increase over the last two decades. India and the Republic of South Africa each produced about equally, 2.6 percent, with about 0.[illegible] percent each from Brazil and Malaysia. World reserves of Zr are tremendous; U.S. reserves alone are greater than the foreseeable demand for the next 100 years, and the substantial reserves in Australia will assure that country's continuing role in world zircon markets.

March 12, 1991
Project No: 400754

APPENDIX F

Zinc Oxide

SY
LINE TOO LONG - DELETED NOT ENOUGH TEAM BUFFERS
RESEND MESSAGE
USER:
PRT DL -8
PROG:

Chemline

Zinc Oxide

8 :
RN - 1314-13-2
ON - 8011-84-5 (CAS)
ON - 8047-36-7 (CAS)
ON - 8047-69-6 (CAS)
ON - 8050-42-8 (CAS)
ON - 8051-03-4 (CAS)
ON - 56592-00-8 (CAS)
ON - 57206-86-7 (CAS)
ON - 78590-82-6 (TOXLINE) (TOXLIT) (MEDLINE) (MED86) (MED80) (MESH)
MF - O-Zn
N1 - Zinc oxide [ZnO] (9CI)
SY - Actox 14 [CAS:HSDB:RTECS]
SY - Actox 16 [CAS:HSDB:RTECS]
SY - Actox 216 [CAS:HSDB:RTECS]
SY - AI3-00277 [HSDB:RTECS]
SY - Amalox [HSDB:RTECS]
SY - AZO 22 [CAS:HSDB]
SY - Azodox [HSDB]
SY - C.I. PIGMENT WHITE 4 [RTECS]
SY - C-Weiss 8 [German] [HSDB]
SY - C-Weiss 8 (Germany) [CTFA]
SY - Cadox XX 78 [CAS:HSDB:RTECS]
SY - Caswell No. 920 [NLM]
SY - CHINESE WHITE [HSDB:RTECS]
SY - CI 77947 [CTFA:HSDB]
SY - CYNKU TLENEK [Polish] [HSDB:RTECS]
SY - Electrox 2500 [CAS:HSDB]
SY - EMANAY ZINC OXIDE [HSDB:RTECS]
SY - EMAR [HSDB:RTECS]
SY - EPA Pesticide Chemical Code 088502 [NLM]
SY - FELLING ZINC OXIDE [HSDB:RTECS]
SY - FLOWERS OF ZINC [HSDB:RTECS]
SY - Germany: C-Weiss 8 [CTFA]
SY - GIAP 10 [CAS:HSDB:RTECS]
SY - GREEN SEAL-8 [HSDB:RTECS]
SY - HSDB 5024 [NLM]
SY - HUBBUCK'S WHITE [HSDB:RTECS]
SY - Kadox 15 [CAS:HSDB:RTECS]
SY - Kadox 72 [CAS:HSDB:RTECS]
SY - KADOX-25 [HSDB:RTECS]
SY - Outmine [CAS:HSDB:RTECS]
SY - OZIDE [HSDB:RTECS]
SY - OZLO [HSDB:RTECS]
SY - PERMANENT WHITE [HSDB:RTECS]
SY - PHILOSOPHER'S WOOL [HSDB:RTECS]
SY - POWDER BASE 900 [HSDB:RTECS]
SY - PROTOX TYPE 166 [HSDB:RTECS]

SY - PROTOX TYPE 167 [HSDB:RTECS]
SY - PROTOX TYPE 168 [HSDB:RTECS]
SY - PROTOX TYPE 169 [HSDB:RTECS]
SY - PROTOX TYPE 267 [HSDB:RTECS]
SY - PROTOX TYPE 268 [HSDB:RTECS]
SY - Protox 166 [CAS:HSDB]
SY - Protox 168 [CAS:HSDB]
SY - Protox 169 [CAS:HSDB]
SY - RED SEAL-9 [HSDB]
SY - SNOW WHITE [HSDB:RTECS]
SY - Unichem ZO [CTFA:HSDB:RTECS]
SY - Vandem VAC [CAS:HSDB:RTECS]
SY - Vandem VOC [CAS:HSDB:RTECS]
SY - Vandem VPC [CAS:HSDB]
SY - WHITE SEAL-7 [HSDB:RTECS]
SY - XX 203 [CAS:HSDB:RTECS]
SY - XX 601 [CAS:HSDB:RTECS]
SY - XX 78 [CAS:HSDB:RTECS]
SY - ZINC MONOXIDE [HSDB]
SY - Zinc oxide (8CI) [CAS:CTFA*:HSDB*:MESH*:RTECS:USPDDN*]
SY - Zinc oxide (ZnO) (9CI) [TSCAINV] [NLM]
SY - Zinc Oxide [USAN] [USPDDN*]
SY - Zinc white [CAS:HSDB:RTECS]
SY - Zinca 20 [CAS:HSDB:RTECS]
SY - Zincoid [HSDB:RTECS]
SY - Zn 0701T [CAS:HSDB:RTECS]
SY - [component of] Caldesene Ointment [USPDDN]
SY - [component of] Dome Paste Bandage [USPDDN]
SY - [component of] Supertah [USPDDN]
SY - [component of] Wyanoids [USPDDN]
SY - [component of] Ziradryl [USPDDN]
[redacted] - Astringent [USPDDN]
CC - Mutation data [RTECS]
CC - Protectant [topical] [USPDDN]
CC - Reproductive Effect [RTECS]
CC - Skin / Eye Irritant [RTECS]
CC - TSCA Flag: XU [TSCAINV]
LO - TOXLINE
LO - TOXLIT
LO - TOXLINE65
LO - TOXLIT65
LO - MEDLINE
LO - MED86
LO - MED83
LO - MED80
LO - MED77
LO - MESH
LO - CANCERLIT
LO - CCRIS
LO - HSDB
LO - RTECS
LO - EINECS
LO - TSCAINV
LO - EMICBACK
LO - ETICBACK
[redacted]M - 9005

AR306695

SS 3 /C?
USER:

NATIONAL LIBRARY OF MEDICINE/TOXNET

NIOSH: REGISTRY OF TOXIC EFFECTS OF CHEMICAL SUBSTANCES [RTECS]

ZINC OXIDE CAS RN = 1314-13-2

1 - RTECS	
RTECS RECORD NUMBER	90417
LAST REVISION DATE	9009
UPDATE HISTORY	Complete Update on 11/01/90, 1 field added/edited/deleted.
UPDATE HISTORY	Complete Update on 08/16/90, 1 field added/edited/deleted.
UPDATE HISTORY	Complete Update on 04/30/90, 1 field added/edited/deleted.
UPDATE HISTORY	Complete Update on 03/08/90, 2 fields added/edited/deleted.
UPDATE HISTORY	Complete Update on 12/11/89, 4 fields added/edited/deleted.
UPDATE HISTORY	Complete Update on 09/01/89, 3 fields added/edited/deleted.
UPDATE HISTORY	Complete Update on 05/11/89, 4 fields added/edited/deleted.
UPDATE HISTORY	Complete Update on 03/24/89, 2 fields added/edited/deleted.
UPDATE HISTORY	Complete Update on 01/25/89, 1 field added/edited/deleted.
UPDATE HISTORY	Complete Update on 10/07/88, 1 field added/edited/deleted.
UPDATE HISTORY	Complete Update on 09/05/88, 1 field added/edited/deleted.
UPDATE HISTORY	Complete Update on 02/03/88, 4 fields added/edited/deleted.
UPDATE HISTORY	Complete Update on 09/12/87, 13 fields added/edited/deleted.
RECORD LENGTH	3943
RTECS ACCESSION NUMBER	NIOSH/ZH4810000
NAME OF SUBSTANCE	**ZINC OXIDE**
CAS REGISTRY NUMBER	**1314-13-2**
OTHER REGISTRY NUMBERS	8051-03-4
OTHER REGISTRY NUMBERS	78590-82-6
SYNONYMS	ACTOX 14
SYNONYMS	ACTOX 16
SYNONYMS	ACTOX 216
SYNONYMS	AI3-00277
SYNONYMS	AKRO-ZINC BAR 85
SYNONYMS	AKRO-ZINC BAR 90
SYNONYMS	AMALOX
SYNONYMS	AZO-33
SYNONYMS	AZO-55
SYNONYMS	AZO-66
SYNONYMS	AZO-77
SYNONYMS	AZODOX-55
SYNONYMS	AZODOX-55TT
SYNONYMS	AZO-55TT

SYNONYMS	AZO-66TT
SYNONYMS	AZO-77TT
SYNONYMS	CADOX XX 78
SYNONYMS	CALAMINE
SYNONYMS	CALAMINE (spray)
SYNONYMS	CHINESE WHITE
SYNONYMS	C.I. 77947
SYNONYMS	C.I. PIGMENT WHITE 4
SYNONYMS	CYNKU TLENEK (Polish)
SYNONYMS	ELEDTROX 2500
SYNONYMS	EMANAY ZINC OXIDE
SYNONYMS	EMAR
SYNONYMS	FELLING ZINC OXIDE
SYNONYMS	FLOWERS OF ZINC
SYNONYMS	GIAP 10
SYNONYMS	GREEN SEAL-8
SYNONYMS	HUBBUCK'S WHITE
SYNONYMS	KADOX 15
SYNONYMS	KADOX-25
SYNONYMS	KADOX 72
SYNONYMS	K-ZINC
SYNONYMS	OUTMINE
SYNONYMS	OZIDE
SYNONYMS	OZLO
SYNONYMS	PASCO
SYNONYMS	PERMANENT WHITE
SYNONYMS	PHILOSOPHER'S WOOL
SYNONYMS	POWDER BASE 900
SYNONYMS	PROTOX TYPE 166
SYNONYMS	PROTOX TYPE 167
SYNONYMS	PROTOX TYPE 168
SYNONYMS	PROTOX TYPE 169
SYNONYMS	PROTOX TYPE 267
SYNONYMS	PROTOX TYPE 268
SYNONYMS	RED-SEAL-9
SYNONYMS	SNOW WHITE
SYNONYMS	UNICHEM ZO
SYNONYMS	VANDEM VAC
SYNONYMS	VANDEM VOC
SYNONYMS	WHITE SEAL-7
SYNONYMS	XX 78
SYNONYMS	XX 203
SYNONYMS	XX 601
SYNONYMS	ZINCA 20
SYNONYMS	ZINCITE
SYNONYMS	ZINCOID
SYNONYMS	ZINC OXIDE (ACGIH,OSHA)
SYNONYMS	ZINC OXIDE FUME
SYNONYMS	ZINC WHITE
SYNONYMS	ZN-0401 E 3/16''
SYNONYMS	Zn 0701T
MOLECULAR FORMULA	O-Zn
MOLECULAR WEIGHT	81.37
CLASSIFICATION CODE	Mutation data
CLASSIFICATION CODE	Reproductive Effect

LASSIFICATION CODE : Skin/Eye Irritant
WISWESSER LINE NOTATION : ZN O
ATA TYPE : Mutagenicity
ATA TYPE : Skin/Eye Irritation
DATA TYPE : General Toxicity
DATA TYPE : Reproductive Studies

UTAGENICITY STUDIES
TEST SYSTEM : DNA damage
SPECIES/ROUTE/ CELL TYPE : E. coli
DOSE : 3000 ppm
REFERENCE : Mutat Res, vol 89, pg 95, 1981 (MUREAV)

MUTAGENICITY STUDIES
TEST SYSTEM : cytogenetic analysis
SPECIES/ROUTE/ CELL TYPE : rat-inhalation
DOSE : 100 ug/m3
REFERENCE : Cytol Genet, vol 12(3), pg 46, 1978 (CYGEDX)

MUTAGENICITY STUDIES
TEST SYSTEM : oncogenic transformation
SPECIES/ROUTE/ CELL TYPE : hamster:embryo
DOSE : 1 mg/L
REFERENCE : Shigaku, vol 74, pg 1385, 1987 (SHIGAZ)

JTAGENICITY STUDIES
TEST SYSTEM : unscheduled DNA synthesis
SPECIES/ROUTE/ CELL TYPE : hamster:embryo
DOSE : 1 mg/L
REFERENCE : Shigaku, vol 74, pg 1385, 1987 (SHIGAZ)

JTAGENICITY STUDIES
TEST SYSTEM : sister chromatid exchange
SPECIES/ROUTE/ CELL TYPE : hamster:embryo
DOSE : 300 ug/L
REFERENCE : Shigaku, vol 74, pg 1385, 1987 (SHIGAZ)

JTAGENICITY STUDIES
TEST SYSTEM : unscheduled DNA synthesis
SPECIES/ROUTE/ CELL TYPE : guinea pig-inhalation
DOSE : 5300 ug/m3/3H/6D
REFERENCE : Toxicol Appl Pharmacol, vol 78, pg 29, 1985 (TXAPA9)

SKIN AND EYE IRRITATION STUDIES
ROUTE : skin
SPECIES : rabbit
DOSE : 500 mg/24H
EFFECT : MILD
REFERENCE : Sb Vysledku Toxikologickeho Vysetreni Latek A Prinpravku 1972, pg 10, 1972 (28ZPAK)

IN AND EYE IRRITATION STUDIES
ROUTE : eye
SPECIES : rabbit
DOSE : 500 mg/24H
EFFECT : MILD

REFERENCE : Sb Vysledku Toxikologickeho Vysetreni Latek A Prinpravku 1972, pg 10, 1972 (28ZPAK)

GENERAL TOXICITY STUDIES
ROUTE : oral
SPECIES : human
STUDY TYPE : LDLo
DOSE : 500 mg/kg
EFFECT : DETAILS NOT REPORTED
REFERENCE : Gekkan Yakuji, vol 22, pg 291, 1980 (YAKUD5)

GENERAL TOXICITY STUDIES
ROUTE : inhalation
SPECIES : human
STUDY TYPE : TCLo
DOSE : 600 mg/m3
EFFECT : LUNGS, THORAX OR RESPIRATION (Cough; Dyspnea; Other changes)
REFERENCE : J Ind Hyg, vol 9, pg 88, 1927 (JIDHAN)

GENERAL TOXICITY STUDIES
ROUTE : intraperitoneal
SPECIES : rat
STUDY TYPE : LD50
DOSE : 240 mg/kg
EFFECT : DETAILS NOT REPORTED
REFERENCE : Zdravookhr Kaz, vol 38(9), pg 18, 1978 (ZDKAA8)

GENERAL TOXICITY STUDIES
ROUTE : oral
SPECIES : mouse
STUDY TYPE : LD50
DOSE : 7950 mg/kg
EFFECT : DETAILS NOT REPORTED
REFERENCE : Gig Sanit, vol 51(4), pg 89, 1986 (GISAAA)

GENERAL TOXICITY STUDIES
ROUTE : inhalation
SPECIES : mouse
STUDY TYPE : LC50
DOSE : 2500 mg/m3
EFFECT : DETAILS NOT REPORTED
REFERENCE : Int Polym Sci Technol, vol 3, pg 93, 1976 (IPSTB3)

REPRODUCTIVE STUDIES
ROUTE : oral
SPECIES : rat
STUDY TYPE : TDLo
DOSE : 6846 mg/kg (1-22D preg)
EFFECT : SPECIFIC DEVELOPMENTAL ABNORMALITIES (Homeostasis)
EFFECT : EFFECTS ON NEWBORN (Stillbirth; Growth statistics)
REFERENCE : J Nutr, vol 98, pg 303, 1969 (JONUAI)

TOXICOLOGY REVIEW TOXICOLOGY REVIEW; ANAEA3 35,165,75; Ann

	Allergy
TOXICOLOGY REVIEW	TOXICOLOGY REVIEW; JIDHAN 8,322,26; J Ind Hyg
THRESHOLD LIMIT VALUE	ACGIH THRESHOLD LIMIT VALUE REVIEW; TWA 10 mg/m3, total dust; 85INA8 5,645,86; Doc Threshold Limit Values
THRESHOLD LIMIT VALUE	ACGIH THRESHOLD LIMIT VALUE REVIEW; TWA 5 mg/m3; STEL 10 mg/m3 (vapor); 85INA8 5,645,86; Doc Threshold Limit Values
NIOSH RECOMMENDED LIMITS	NIOSH REL TO ZINC OXIDE-air:10H TWA 5 mg/m3;CL 15 mg/m3/15M; MMWR** 37(S-7),29,88; Morbid Mortal Weekly Rep
NIOSH EXPOSURE SURVEYS	NATIONAL OCCUPATIONAL EXPOSURE SURVEY 1983: Hazard#: X5686; number of industries: 289; total number of facilities: 53566; number of occupations: 168; total number of employees: 828976; total number of female employees: 122696
STANDARDS AND REGULATIONS	EPA FIFRA 1988 PESTICIDE SUBJECT TO REGISTRATION OR RE-REGISTRATION; FEREAC 54,4388,89; Fed Regist
STANDARDS AND REGULATIONS	MSHA STANDARD-air:TWA 5 mg/m3 (fume); DTLVS* 3,284,71; Doc Threshold Limit Values
STANDARDS AND REGULATIONS	OSHA PEL:8H TWA 5 mg/m3, fume and respirable fraction; FEREAC 54,2923,89; Fed Regist
STANDARDS AND REGULATIONS	OSHA PEL:8H TWA 15 mg/m3, total dust; FEREAC 54,2923,89; Fed Regist
STANDARDS AND REGULATIONS	OSHA PEL FINAL:8H TWA 5 mg/m3;STEL 10 mg/m3, fume; FEREAC 54,2923,89; Fed Regist
STANDARDS AND REGULATIONS	OSHA PEL FINAL:8H TWA 10 mg/m3, total dust; FEREAC 54,2923,89; Fed Regist
STANDARDS AND REGULATIONS	OSHA PEL FINAL:8H TWA 5 mg/m3, respirable fraction; FEREAC 54,2923,89; Fed Regist
FEDERAL PROGRAM STATUS	EPA TSCA CHEMICAL INVENTORY, JUNE 1990
FEDERAL PROGRAM STATUS	EPA TSCA TEST SUBMISSION (TSCATS) DATA BASE, SEPTEMBER 1990
FEDERAL PROGRAM STATUS	NIOSH ANALYTICAL METHODS: see ZINC, 7030; ZINC OXIDE, 7502
FEDERAL PROGRAM STATUS	OSHA ANALYTICAL METHOD #ID-143
FEDERAL PROGRAM STATUS	OSHA ANALYTICAL METHOD #ID-125G

NATIONAL LIBRARY OF MEDICINE/TOXNET

CHEMICAL CARCINOGENESIS RESEARCH INFORMATION SYSTEM [CCRIS]

ZINC OXIDE CAS RN = 1314-13-2

1- CCRIS
CHEMICAL CARCINOGENESIS RECORD NUMBER 1309
LAST REVISION DATE 851231
UPDATE HISTORY Complete Update on 12/31/85
RECORD LENGTH 518
NAME OF SUBSTANCE ZINC OXIDE
CAS REGISTRY NUMBER 1314-13-2
DATA TYPE Mutagenicity
MUTAGENICITY STUDIES
TEST SYSTEM : MOUSE LYMPHOMA
STRAIN/INDICATOR : L5178Y (TK+/TK-)
METABOLIC ACTIVATION : RAT, LIVER, S-9, AROCLOR 1254
METHOD : SUSPENSION/PLATE
DOSE RANGE : 5.0-24 UG/ML
RESULTS : POSITIVE
REFERENCE : [SHORT-TERM TEST PROGRAM SPONSORED BY THE DIVISION OF CANCER ETIOLOGY, NATIONAL CANCER INSTITUTE, DR. THOMAS P. CAMERON, PROJECT OFFICER , Y82]

MUTAGENICITY STUDIES
TEST SYSTEM : MOUSE LYMPHOMA
STRAIN/INDICATOR : L5178Y (TK+/TK-)
METABOLIC ACTIVATION : NONE
METHOD : SUSPENSION/PLATE
DOSE RANGE : 1.0-4.9 UG/ML
RESULTS : POSITIVE
REFERENCE : [SHORT-TERM TEST PROGRAM SPONSORED BY THE DIVISION OF CANCER ETIOLOGY, NATIONAL CANCER INSTITUTE, DR. THOMAS P. CAMERON, PROJECT OFFICER , Y82]

NATIONAL LIBRARY OF MEDICINE/TOXNET

HAZARDOUS SUBSTANCES DATABANK [HSDB]
(Some data in this file may not be peer reviewed.)

ZINC OXIDE CAS RN = 1314-13-2

1 - HSDB	
HAZARDOUS SUBSTANCES DATABANK NUMBER	5024
LAST REVISION DATE	901023
REVIEW DATE	Reviewed by SRP on 5/20/88
UPDATE HISTORY	Complete Update on 10/23/90, 1 field added/edited/deleted.
UPDATE HISTORY	Complete Update on 05/21/90, 2 fields added/edited/deleted.
UPDATE HISTORY	Field Update on 01/15/90, 1 field added/edited/deleted.
UPDATE HISTORY	Complete Update on 01/11/90, 2 fields added/edited/deleted.
UPDATE HISTORY	Complete Update on 04/05/89, 65 fields added/edited/deleted.
UPDATE HISTORY	Complete Update on 01/13/85
RECORD LENGTH	72054
NAME OF SUBSTANCE	**ZINC OXIDE**
CAS REGISTRY NUMBER	**1314-13-2**
SYNONYMS	ACTOX 14 **PEER REVIEWED**
SYNONYMS	ACTOX 16 **PEER REVIEWED**
SYNONYMS	ACTOX 216 **PEER REVIEWED**
SYNONYMS	AMALOX **PEER REVIEWED**
SYNONYMS	AZODOX **PEER REVIEWED**
SYNONYMS	AZO 22 **PEER REVIEWED**
SYNONYMS	CADOX XX 78 **PEER REVIEWED**
SYNONYMS	CHINESE WHITE **PEER REVIEWED**
SYNONYMS	CI 77947 **PEER REVIEWED**
SYNONYMS	CI PIGMENT WHITE 4 **PEER REVIEWED**
SYNONYMS	CYNKU TLENEK (POLISH) **PEER REVIEWED**
SYNONYMS	EMANAY ZINC OXIDE **PEER REVIEWED**
SYNONYMS	EMAR **PEER REVIEWED**
SYNONYMS	FELLING ZINC OXIDE **PEER REVIEWED**
SYNONYMS	FLORES DE ZINCI **PEER REVIEWED**
SYNONYMS	FLOWERS OF ZINC **PEER REVIEWED**
SYNONYMS	GREEN SEAL-8 **PEER REVIEWED**
SYNONYMS	HUBBUCK'S WHITE **PEER REVIEWED**
SYNONYMS	KADOX 15 **PEER REVIEWED**
SYNONYMS	KADOX 72 **PEER REVIEWED**
SYNONYMS	KADOX-25 **PEER REVIEWED**
SYNONYMS	OZIDE **PEER REVIEWED**
SYNONYMS	OZLO **PEER REVIEWED**
SYNONYMS	PERMANENT WHITE **PEER REVIEWED**
SYNONYMS	PHILOSOPHER'S WOOL **PEER REVIEWED**
SYNONYMS	POWDER BASE 900 **PEER REVIEWED**
SYNONYMS	PROTOX TYPE 166 **PEER REVIEWED**
SYNONYMS	PROTOX TYPE 167 **PEER REVIEWED**

SYNONYMS PROTOX TYPE 168 **PEER REVIEWED**
SYNONYMS PROTOX TYPE 169 **PEER REVIEWED**
SYNONYMS PROTOX TYPE 267 **PEER REVIEWED**
SYNONYMS PROTOX TYPE 268 **PEER REVIEWED**
SYNONYMS RED SEAL-9 **PEER REVIEWED**
SYNONYMS SNOW WHITE **PEER REVIEWED**
SYNONYMS VANDEM VAC **PEER REVIEWED**
SYNONYMS VANDEM VOC **PEER REVIEWED**
SYNONYMS VANDEM VPC **PEER REVIEWED**
SYNONYMS WHITE SEAL-7 **PEER REVIEWED**
SYNONYMS XX 203 **PEER REVIEWED**
SYNONYMS XX 78 **PEER REVIEWED**
SYNONYMS ZINC MONOXIDE **PEER REVIEWED**
SYNONYMS ZINC WHITE **PEER REVIEWED**
SYNONYMS ZINCA 20 **PEER REVIEWED**
SYNONYMS ZINCOID **PEER REVIEWED**
SYNONYMS ZN 0701T **PEER REVIEWED**
SYNONYMS AI3-00277 **PEER REVIEWED**
SYNONYMS C-Weiss 8 (German) **PEER REVIEWED**
SYNONYMS Caswell No 920 **PEER REVIEWED**
SYNONYMS Electrox 2500 **PEER REVIEWED**
SYNONYMS EPA Pesticide Chemical Code 088502 **PEER REVIEWED**
SYNONYMS GIAP 10 **PEER REVIEWED**
SYNONYMS Blanc de Zinc **PEER REVIEWED**
SYNONYMS Zincum Oxydatum **PEER REVIEWED**
SYNONYMS Zinci Oxydum **PEER REVIEWED**
SYNONYMS Zinci Oxicum **PEER REVIEWED**
SYNONYMS Outmine **PEER REVIEWED**
SYNONYMS Protox 166 **PEER REVIEWED**
SYNONYMS Protox 168 **PEER REVIEWED**
SYNONYMS Protox 169 **PEER REVIEWED**
SYNONYMS Unichem ZO **PEER REVIEWED**
SYNONYMS XX 601 **PEER REVIEWED**
MOLECULAR FORMULA O-Zn **PEER REVIEWED**
RTECS NUMBER NIOSH/ZH4810000
RELATED HSDB RECORDS 1344 [ZINC]

METHODS OF MANUFACTURING

... BY VAPORIZATION OF METALLIC ZINC & OXIDATION OF VAPORS WITH PREHEATED AIR (FRENCH PROCESS); ALSO FROM FRANKLINITE, (AMERICAN PROCESS) OR FROM ZINC SULFIDE: FAITH, KEYES, & CLARK'S INDUST CHEM (WILEY, NEW YORK, 4TH ED, 1975) PAGES 882-888. [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**

METHODS OF MANUFACTURING

Oxidation of vapor-fractionated die castings [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1255] **PEER REVIEWED**

IMPURITIES

... Some technical grades contain a few tenths of a percent lead. [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. II-142] **PEER REVIEWED**

IMPURITIES

Zinc oxide shall conform to the following specifications and

shall be free from impurities other than those named to the extent that such impurities may be avoided by good manufacturing practice: Zinc oxide (as ZnO), not less than 99 ppm. Loss on ignition at 800 deg C, not more than 1 percent. Cadmium (as Cd), not more than 15 ppm. Mercury (as Hg), not more than 1 ppm. Arsenic (as As), not more than 3 ppm. Lead (as Pb), not more than 20 ppm. [21 CFR 73.1991 (4/1/86)] **PEER REVIEWED**

FORMULATIONS/PREPARATIONS

ZINC OXIDE IS INCORPORATED IN POWDERS, OINTMENTS, & PASTES. ... PREPN CONTAINING ZINC OXIDE INCL ZINC OXIDE OINTMENT (20% OR 25% ZNO), ZINC OXIDE PASTE (25% ZNO), & ZINC OXIDE & SALICYLIC ACID PASTE (2% SALICYLIC ACID IN ZINC OXIDE PASTE). [Gilman, A.G., L.S.Goodman, and A. Gilman. (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 7th ed. New York: Macmillan Publishing Co., Inc., 1985. , p. 967] **PEER REVIEWED**

)RMULATIONS/PREPARATIONS

CALAMINE CONSISTS OF PINK POWDER CONTAINING ZINC OXIDE (NOT LESS THAN 98%) & SMALL AMT OF FERRIC OXIDE. IT IS INCORPORATED INTO CALAMINE LOTION (8% CALAMINE & 8% ZINC OXIDE), & PHENOLATED CALAMINE LOTION (CMPD CALAMINE LOTION) (1% PHENOL IN CALAMINE LOTION). [Gilman, A.G., L.S.Goodman, and A. Gilman. (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 7th ed. New York: Macmillan Publishing Co., Inc., 1985. , p. 967] **PEER REVIEWED**

FORMULATIONS/PREPARATIONS

GRADES: DEPEW, USA PATENT 2,372,367 (1945 TO AMERICAN ZINC, LEAD & SMELTING). MEDICINAL GRADE CONTAINS 99.5% OR MORE ZINC OXIDE; TECHNICAL GRADES CONTAIN 90-99% ZINC OXIDE & A FEW TENTHS OF 1% OF LEAD. [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**

I)RMULATIONS/PREPARATIONS

GRADES: AMERICAN PROCESS, LEAD-FREE; FRENCH PROCESS, LEAD-FREE, GREEN SEAL, RED SEAL, WHITE SEAL (ACCORDING TO FINENESS); LEADED (WITH LEAD SULFATE); USP, SINGLE CRYSTALS. [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1255] **PEER REVIEWED**

F)RMULATIONS/PREPARATIONS

Topical ointment 20%, paste 25% (Available by nonproprietary name) [ASHP. American Hospital Formulary Service - Drug Information 87. Bethesda, MD: American Society of Hospital Pharmacists, 1987. (Plus Supplements, 1987) , p. 1947] **PEER REVIEWED**

F RMULATIONS/PREPARATIONS

Zinc oxide preparations: Bandages: Zinc Paste and Coal Tar Bandage ... not less than 6% zinc oxide; Zinc Paste and Ichthammol Bandage ... zinc oxide 6.25 g per 100 g; Zinc Paste Bandge ... not less than 6% zinc oxide; Zinc Paste, Calamine and Clioquinol Bandage ... zinc oxide 9.25 g per 100 g; Creams: Zinc and Ichthammol Cream ... zinc cream 82 g per 100 g; Zinc Cream ... zinc oxide 32 g per 100 g; Zinc Cream Oily ... zinc oxide 32 g per 100 g; Zinc Oxide and Diphenhydramine Cream ... zinc oxide 8 g per 100 g; Dental Cements: Zinc-Eugenol Cement; Kerr's Sealer; Dental Paste: Dental Triozinc Paste;

Dusting-powders: Cmpd Zinc Dusting-powder; Conspergens Zinci; Zinc and Salicylic Acid Dusting-powder; Zinc, Starch, and Talc Dusting-powder; Gauzes: Zinc Gelatin Impregnated Gauze; Liniments: Linimentum Phenoli et Zinci Oxydi; Linimentum Zinci; Lotions: Lotions F; Schamberg's Lotion; Zinc Talc Lotion; Ointments: Hamer's Hemorrhoidal Ointment; Zinc and Caster Oil Ointment; Zinc Ointment; Zinc Oxide and Ichthammol Ointment; Zinc oxide cmpd ointment; Pastes: Cmpd Zinc Paste; Zinc Gelatin [Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. , p. 509] **PEER REVIEWED**

FORMULATIONS/PREPARATIONS

Proprietary preparations: Calaband, Coltapaste, Ichthopaste, Icthaband, Noratex, Pharmakon, Quinaband, Septex Cream No1, Sudocrem, Tarband, Thovaline, Impregnated Gauze, Viscopaste, Viscopaste PB7, Zincaband; Herisan; Oxyplastine [Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. , p. 510] **PEER REVIEWED**

MANUFACTURERS

American Chemet Corp, Hq, 400 County Line Rd, Deerfield, IL 60015, (312) 948-0800; Production site: East Helena, MT 59635 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1066] **UNREVIEWED**

MANUFACTURERS

ASARCO Inc, Hq, 180 Maiden Ln, New York, NY 10038, (212) 510-2000; Production site: Hillsboro, IL 62049 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1066] **UNREVIEWED**

MANUFACTURERS

TL Diamond & Co, Inc, Hq, 30 Rockefeller Center, New York, NY 10112, (212) 582-0420; Production site: Hillsboro, IL 62049 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1066] **UNREVIEWED**

MANUFACTURERS

Gulf Metals Industries, Inc, Hq, 6020 Esperson, Houston, TX 77001, (713) 926-1705; Midwest Zinc Corp, 1001 Weed St, Chicago, IL 60622 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1066] **UNREVIEWED**

MANUFACTURERS

Horsehead Industries, Inc, Hq, 204 E 39th St, New York, NY 10017, (212) 972-2100; Subsidiary: Zinc Corp of America, 300 Frankfurt Rd, Route 18, Monaca, PA 15061-2295, (412) 774-1020; Production sites: Monaca, PA 15061; Palmerton, PA 18071 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1067] **UNREVIEWED**

MANUFACTURERS

Inland Zinc, Hq, Spokane Industrial Park, PO Box 323, Veradale, WA 99037, (509) 924-0243 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI

International, 1989. , p. 1067] **UNREVIEWED**

MANUFACTURERS

PASCO Zinc Corp, Hq, 22219 South Western Ave, Torrance, CA 90510, (213) 775-3421; Production site: Millington, TN 38053 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1067] **UNREVIEWED**

MANUFACTURERS

Philipp Brothers Chemicals, Inc, Hq, One Parker Plaza, Fort Lee, NJ 07024, (201) 944-6020; Subsidiary: The Prince Manufacturing Co; Production sites: Bowmanstown, PA 18030; Radio Rd, Qunicy, IL 62306 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1067] **UNREVIEWED**

MANUFACTURERS

United Catalysts Inc, Hq, 1227 South 12th St, Louisville, KY 40232, (502) 634-7200; Production site: Louisville, KY 40201 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1067] **UNREVIEWED**

MAJOR USES

AS PIGMENT IN WHITE PAINT INSTEAD OF LEAD CARBONATE; IN COSMETICS, DRIERS, QUICK-SETTING CEMENTS; WITH SYRUPY PHOSPHORIC ACID OR ZNCL2 IN DENTAL CEMENTS; MFR OF OPAQUE GLASS & CERTAIN TYPES OF TRANSPARENT GLASS; MFR ENAMELS, AUTOMOBILE TIRES, WHITE GLUE, MATCHES, WHITE PRINTING INKS, PORCELAINS, ZINC GREEN; AS REAGENT IN ANAL CHEM; IN ELECTROSTATIC COPYING PAPER; AS FLAME RETARDANT; IN ELECTRONICS AS SEMICONDUCTOR [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**

MAJOR USES

MEDICATION: ASTRINGENT, TOPICAL PROTECTANT; MEDICATION (VET): ANTISEPTIC, ASTRINGENT, PROTECTIVE (TOPICAL) [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**

MAJOR USES

ACCELERATOR ACTIVATOR & REINFORCING AGENT IN RUBBER; OINTMENTS; PIGMENT & MOLD GROWTH INHIBITOR IN PAINTS; IN FLOOR TILE; FEED ADDITIVE; DIETARY SUPPLEMENT; SEED TREATMENT; PIEZOELECTRIC DEVICES; PHOTOCONDUCTOR IN OFFICE COPYING MACHINES & IN COLOR PHOTOGRAPHY [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1255] **PEER REVIEWED**

MAJOR USES

(VET): ... USED AS FEED ADDITIVE SOURCE OF ZINC. ITS BIOLOGICAL AVAILABILITY SEEMS ADEQUATE FOR CATTLE, SWINE & CHICKENS, BUT MAY BE POOR FOR POULTS. [Rossoff, I.S. Handbook of Veterinary Drugs. New York: Springer Publishing Company, 1974. , p. 668] **PEER REVIEWED**

MAJOR USES

ORAL USE IN CATTLE CONTROLS DEVELOPMENT OF HORN FLY & FACE FLY LARVAE IN MANURE. AN INSECTICIDAL ADJUVANT OFTEN USED IN HIGH CONCN AGAINST SCREWWORMS & EAR TICKS. ITS USE IN MANY CMPD HELPS MAKE THEM MILDEW RESISTANT. [Rossoff, I.S. Handbook of Veterinary Drugs. New York: Springer Publishing Company, 1974.

, p. 668] **PEER REVIEWED**

MAJOR USES
Zinc oxide was used in floor covering, fabrics, lubricants, plastics, and rayon manufacture. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2035] **PEER REVIEWED**

AJOR USES
As dusting powder [Gilman, A.G., L.S.Goodman, and A. Gilman. (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 7th ed. New York: Macmillan Publishing Co., Inc., 1985. , p. 948] **PEER REVIEWED**

MAJOR USES
In carbon black mixtures [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 4(78) 638] **PEER REVIEWED**

I AJOR USES
As anticaking agent [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 7(79) 283] **PEER REVIEWED**

I AJOR USES
In dental disclosing waxes [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 7(79) 512] **PEER REVIEWED**

I AJOR USES
In elastomer curing [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 8(79) 497] **PEER REVIEWED**

MAJOR USES
In electrical insulation [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 13(81) 565] **PEER REVIEWED**

MAJOR USES
As grease filler [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 14(81) 503] **PEER REVIEWED**

MAJOR USES
In hydrogen manufacture [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 12(80) 968] **PEER REVIEWED**

I AJOR USES
In hydrogen sulfide absorber cartridge [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 3(78) 550] **PEER REVIEWED**

MAJOR USES
In polybutadiene curing [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 8(79) 560] **PEER REVIEWED**

MAJOR USES
Polycrystalline zinc oxide, with Bi2O3 and other additives, has nonohmic conduction and is used as a voltage-dependent resistor (varistor) to protect electronic equipment against voltage surges. [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons,

1978-1984. 5(79) 309] **PEER REVIEWED**

MAJOR USES
As drug colorants (external use only) [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 6(79) 568] **PEER REVIEWED**

MAJOR USES
As dental material: zinc oxide-eugenol impression pastes [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 7(79) 498] **PEER REVIEWED**

AJOR USES
The first polychloroprene was vulcanized compounding with zinc oxide, sulfur, stearic acid, piperidiniumpentamethylenedithiocarbamate, and antioxidant [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 8(79) 523] **PEER REVIEWED**

AJOR USES
In electrofax process- zinc oxide powder is dye-sensitized by adsorption to extend its photosensitivity across the visible region [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 8(79) 813] **PEER REVIEWED**

AJOR USES
In SAW (Strike-Anywhere) match [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 15(81) 6] **PEER REVIEWED**

R USES
Zinc, one of the most widely used micronutrients, is applied as sulfates (both basic and normal hydrates), carbonate, sulfide, phosphate, oxide, chelates, and other organic materials. Rates of application range from 0.2 to 2 kg zinc/hr sq m. [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 10(80) 82] **PEER REVIEWED**

MAJOR USES
Zinc oxide: zinc is the most commonly used phosphor powder in vacuum fluorescence displays [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 7(79) 748] **PEER REVIEWED**

AJOR USES
Zinc oxide bed is used to remove mercaptans, hydrogen sulfide and to some extent chlorine at temperatures of 350-400 deg C [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 2(78) 488] **PEER REVIEWED**

MAJOR USES
Zinc oxide may be safely used in cosmetics, including cosmetics intended for use in the area of the eye, in amounts consistent with good manufacturing practice. [21 CFR 73.2991 (4/1/86)] **PEER REVIEWED**

AJOR USES
The color additive zinc oxide may be safely used for coloring externally applied drugs, including those used in the area of the eye, in amounts consistent with good manufacturing

practice. [21 CFR 73.1991 (4/1/86)] **PEER REVIEWED**

CONSUMPTION PATTERNS

Rubber, 50%; agriculture, 15%; chemicals, 12%; paints, 8%; ceramics, 5%; photocopying, 5%; miscellaneous, 5% (1986) [CHEMICAL PRODUCTS SYNOPSIS: Zinc Oxide, 1987] **PEER REVIEWED**

U.S. PRODUCTION

(1986) 1.30X10+11 g [CHEMICAL PRODUCTS SYNOPSIS: Zinc Oxide, 1987] **PEER REVIEWED**

U.S. IMPORTS

(1986) 4.36X10+10 g [CHEMICAL PRODUCTS SYNOPSIS: Zinc Oxide, 1987] **PEER REVIEWED**

U.S. EXPORTS

(1986) 9.08X10+8 g [CHEMICAL PRODUCTS SYNOPSIS: Zinc Oxide, 1987] **PEER REVIEWED**

COLOR/FORM	WHITE OR YELLOWISH-WHITE POWDER, OR HEXAGONAL CRYSTALS [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**
COLOR/FORM	COARSE GRAYISH POWDER [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1255] **PEER REVIEWED**
ODOR	ODORLESS [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**
TASTE	BITTER TASTE [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1255] **PEER REVIEWED**
MELTING POINT	1975 DEG C [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-144] **PEER REVIEWED**
MOLECULAR WEIGHT	81.38 [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-144] **PEER REVIEWED**
DENSITY/SPECIFIC GRAVITY	5.607 AT 20 DEG C/4 DEG C [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**
PH	6.95 (AMERICAN PROCESS ZINC OXIDE); 7.37 (FRENCH PROCESS) [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**
SOLUBILITIES	SOL IN DIL ACETIC OR MINERAL ACIDS, AMMONIA, AMMONIUM CARBONATE, FIXED ALKALI HYDROXIDE SOLN. ... [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**
SOLUBILITIES	SOL IN AMMONIUM CHLORIDE; INSOL IN ALC [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida:

	CRC Press Inc., 1987-1988. B-144] **PEER REVIEWED**
UBILITIES	0.00016 G/100 CC WATER AT 29 DEG C [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-144] **PEER REVIEWED**
SPECTRAL PROPERTIES	INDEX OF REFRACTION: 2.0041, 2.0203 [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**
SPECTRAL PROPERTIES	INDEX OF REFRACTION: 2.008, 2.029 [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-144] **PEER REVIEWED**
OTHER CHEMICAL/PHYSICAL PROPERTIES	HAS GREATEST UV ABSORPTION OF ALL COMMERCIAL PIGMENTS [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1255] **PEER REVIEWED**
OTHER CHEMICAL/PHYSICAL PROPERTIES	WHEN STRONGLY HEATED IT ASSUMES A YELLOW COLOR WHICH DISAPPEARS ON COOLING [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975. , p. 719] **PEER REVIEWED**
OTHER CHEMICAL/PHYSICAL PROPERTIES	ZINC OXIDE IS OPAQUE TO ALL WAVELENGTHS OF LIGHT [American Medical Association, AMA Department of Drugs. AMA Drug Evaluations. 4th ed. Chicago: American Medical Association, 1980. , p. 1015] **PEER REVIEWED**
OTHER CHEMICAL/PHYSICAL PROPERTIES	VERY FINE, AMORPHOUS, WHITE OR YELLOWISH-WHITE POWDER WHICH IS FREE FROM GRITTY PARTICLES [ASHP. American Hospital Formulary Service - Drug Information 87. Bethesda, MD: American Society of Hospital Pharmacists, 1987. (Plus Supplements, 1987) , p. 1945] **PEER REVIEWED**
OTHER CHEMICAL/PHYSICAL PROPERTIES	INCOMPATIBILITIES: REACTS SLOWLY WITH FATTY ACIDS IN OILS & FATS TO PRODUCE LUMPY MASSES OF ZINC OLEATE, STEARATE, ETC. [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975. , p. 719] **PEER REVIEWED**
OTHER CHEMICAL/PHYSICAL PROPERTIES	Zinc oxide form cement-like products when mixed with a strong soln of zinc chloride or with phosphoric acid, owing to the formation of oxy-salts; When ointments containing zinc oxide and water were melted and exposed to UV light, hydrogen

peroxide was produced, in the case of fatty ointments containing cholesterol, amt of hydrogen peroxide was less and the cholesterol was partly oxidized. [Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. , p. 509] **PEER REVIEWED**

OTHER CHEMICAL/PHYSICAL PROPERTIES
Heat capacity: 40.26 J/mol deg C at 25 deg C; coefficient of expansion: 4.0X10-6/deg C; conductivity: 25.2 W/mK; magnetic susceptibility: 0.20X10-6 Hz units [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 24(84) 854] **PEER REVIEWED**

EACTIVITIES & INCOMPATIBILITIES
Slow addition of zinc white (a voluminous oxide containing much air) to cover the surface of linseed oil varnish caused generation of heat and ignition. [Bretherick, L. Handbook of Reactive Chemical Hazards. 3rd ed. Boston, MA: Butterworths, 1985. , p. 1337] **PEER REVIEWED**

EACTIVITIES & INCOMPATIBILITIES
Reacts with hydrochloric acid to produce zinc chloride. [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1252] **PEER REVIEWED**

EACTIVITIES & INCOMPATIBILITIES
Reacts with sulfuric acid to produce zinc sulfate. [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1257] **PEER REVIEWED**

EACTIVITIES & INCOMPATIBILITIES
Zinc oxide reacts with hydrogen fluoride to prepare zinc fluoride tetrahydrate. [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 10(80) 826] **PEER REVIEWED**

EACTIVITIES & INCOMPATIBILITIES
Zinc oxide reacts with carbon monoxide or hydrogen to produce /elemental zinc/. [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 24(84) 855] **PEER REVIEWED**

REACTIVITIES & INCOMPATIBILITIES
... Zinc oxide is ... reduced explosively /with magnesium/ on heating. [Bretherick, L. Handbook of Reactive Chemical Hazards. 3rd ed. Boston, MA: Butterworths, 1985. , p. 1269] **PEER REVIEWED**

EACTIVITIES & INCOMPATIBILITIES
ZINC OXIDE POWDER REACTS VIOLENTLY WITH CHLORINATED RUBBER AT 215 DEG C. [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1255] **PEER REVIEWED**

PROTECTIVE EQUIPMENT & CLOTHING
Respirator selection: upper limit devices recommended by OSHA: 50 mg/cu m: any dust, mist, and fume respirator with a full

facepiece or any supplied air respirator or any self-contained breathing apparatus; 125 mg/cu m: any powered air-purifying respirator with a dust, mist, and fume filter or any supplied-air respirator operated in a continuous flow mode; 250 mg/cu m: any air-purifying full facepiece respirator with a high-efficiency particulate filter or any powered air-purifying respirator with a tight-fitting facepiece and a high-efficiency particulate filter or any self-contained breathing apparatus with a full facepiece or any supplied-air respirator with a full facepiece or any supplied-air respirator with a tight-fitting facepiece operated in a continuous flow mode; 2500 mg/cu m: any supplied-air repirator with a full facepiece and operated in a pressure-demand or other positive pressure mode; Emergency or planned entry in unknown concn or IDLH conditions: any self-contained breathing apparatus with a full facepiece and operated in a pressure-demand or other positive pressure mode or any supplied-air respirator with a full facepiece and operated in a pressure-demand or other positive pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode ; Escape: any air-purifying full facepiece respirator with a high-efficiency particulate filter or any appropriate escape-type self-contained breathing apparatus /Zinc oxide fume/ [NIOSH. Pocket Guide to Chemical Hazards. 5th Printing/Revision. DHHS (NIOSH) Publ. No. 85-114. Washington, D.C.: U.S. Dept. of Health and Human Services, , p. 239] **PEER REVIEWED**

R PREVENTIVE MEASURES

In all cases where zinc is heated to the point where fume is produced, it is most important to ensure that adequate ventilation is provided. Individual protection is best ensured by education of the worker concerning metal-fume fever & the provision of local exhaust ventilation, or, in some situations by wearing of supplied-air hood or mask. /Zinc compounds/ [International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. , p. 2342] **PEER REVIEWED**

IIPMENT METHODS AND REGULATIONS

Whenever hazardous materials are to be transported, Title 49 CFR, Transportation, Parts 100-180, published by the US Dept of Transportation, contain the regulatory requirements and must be consulted. [52 FR 16482 (5/5/87)] **PEER REVIEWED**

STORAGE CONDITIONS

Store in airtight containers. [Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. , p. 509] **PEER REVIEWED**

DISPOSAL METHODS

SRP: At the time of review, criteria for land treatment or burial (sanitary landfill) disposal practices are subject to significant revision. Prior to implementing land disposal of waste residue (including waste sludge), consult with environmental regulatory agencies for guidance on acceptable disposal practices. [CITATION] **PEER REVIEWED**

OSAL METHODS

Chemical Treatability of Zinc; Concentration Process: Chemical

precipitation; Chemical Classification: Metals; Scale of Study: Literature review; Type of Wastewater Used: Unknown; Results of Study: 10.6% reduction by sedimentation. /Zinc cmpd/ [USEPA; Management of Hazardous Waste Leachate, EPA Contract No. 68-03-2766 p.E-75 (1982)] **PEER REVIEWED**

DISPOSAL METHODS

Chemical Treatability of Zinc; Concentration Process: Reverse osmosis; Chemical Classification: Metals; Scale of Study: Batch flow; Type of Wastewater Used: Pure compound (one solute in a solvent); Results of Study: 96.6% reduction with C/PEI membrane at pH= 8.0 100% recution with C/PEI membrane at pH= 11.0; CA membrane operated at 400 psig and 16-22 deg C. /Zinc cmpd/ [USEPA; Management of Hazardous Waste Leachate, EPA Contract No. 68-03-2766 p.E-88 (1982)] **PEER REVIEWED**

ISPOSAL METHODS

Chemical Treatability of Zinc; Concentration Process: Reverse osmosis; Chemical Classification: Metals; Scale of Study: Batch flow; Type of Wastewater Used: Pure compound (one solute in a solvent); Results of Study: 96.9-99.5% reduction with CA membrane; CA membrane operated at 400 psig and 16-22% deg C. /Zinc cmpd/ [USEPA; Management of Hazardous Waste Leachate, EPA Contract No. 68-03-2766 p.E-88 (1982)] **PEER REVIEWED**

DISPOSAL METHODS

Landfill: Dispose of scrap in an approved sanitary landfill in accordance with local regulations. [United Nations. Treatment and Disposal Methods for Waste Chemicals (IRPTC File). Data Profile Series No. 5. Geneva, Switzerland: United Nations Environmental Programme, Dec. 1985. , p. 303] **QC REVIEWED**

TABILITY/SHELF LIFE

GRADUALLY ABSORBS CARBON DIOXIDE UPON EXPOSURE TO AIR [ASHP. American Hospital Formulary Service - Drug Information 87. Bethesda, MD: American Society of Hospital Pharmacists, 1987. (Plus Supplements, 1987) , p. 1945] **PEER REVIEWED**

TABILITY/SHELF LIFE

SUBLIMES AT NORMAL PRESSURE [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1457] **PEER REVIEWED**

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THE FOLLOWING APPEARS TO BE GENERIC FOR ZINC COMPOUNDS.

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MERGENCY MEDICAL TREATMENT

o LIFE SUPPORT :

This overview assumes that basic life support measures have been instituted.

CLINICAL EFFECTS :

SUMMARY

- o Symptoms below are listed by route not symptom category.

Zinc chloride will be similar to a strong acid. Symptoms of inhalation of zinc may start in 3 to 10 hours, and produce symptoms of flu which usually abate in 24 to 48 hours.

RESPIRATORY

- Inhalation of soldering fume containing **zinc chloride** may cause asthma.

GASTROINTESTINAL

- INGESTION: **Zinc salts** produce gastritis ranging from a burning pain in the mouth and throat caused by zinc sulfate, to intense gastric and substernal pain, violent vomiting, diarrhea, shock, and possible death caused from **zinc chloride, phosphide, and sulfate**. Strictures and nephritis have been reported.
- **Zinc** for treating acne has produced hemorrhagic gastritis resulting in anemia.

LABORATORY :

- Tests are available to qualitatively and quantitatively evaluate **zinc**, but these are of little value in treatment.

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o TREATMENT OVERVIEW :

ORAL EXPOSURE

- **Zinc chloride and phosphide** are highly corrosive and emesis or gastric lavage should be avoided. Emesis should be initiated following ingestion of dietary supplements containing **zinc sulfate** unless the patient is already vomiting or if there is evidence of oral mucosal burns.
- With corrosive **zinc salts**, dilute rapidly with water or milk.
- **Zinc** and aluminum **phosphide** will release phosphine gas in the stomach if they come in contact with water. If ipecac is administered, it should perhaps not be followed with fluids. Gastric lavage may also be dangerous. If activated charcoal is administered, it should perhaps be mixed with sorbitol and not water.
- DILUTION: Immediately dilute with 4 to 8 ounces (120 to 240 mL) of milk or water (not to exceed 15 mL/kg in a child).
- EMESIS: May be indicated in recent substantial ingestion unless the patient is or could rapidly become obtunded, comatose or convulsing. Is most effective if initiated within 30 minutes. (Dose of Ipecac Syrup: ADULT: 30 mL; CHILD 1 to 12 years: 15 mL).
- ACTIVATED CHARCOAL/CATHARTIC: Administer charcoal slurry, aqueous or mixed with saline cathartic or sorbitol. Usual charcoal dose: 30 to 100 g in adults and 15 to 30 g in children (1 to 2 g/kg in infants). Administer one dose of a cathartic, mixed with charcoal or given separately. See Section 5.3.1. for doses.
- Give calcium disodium edetate orally and IV, or BAL intramuscularly.

- SUPPORTIVE CARE: Maintain hydration and observe for metabolic acidosis, hypocalcemic tetany, anuria, liver damage, gastric perforation and pyloric stenosis.

INHALATION EXPOSURE

- Metal Fume Fever, most often caused by welding galvanized metal (**ZNO**), is a brief, self-limiting illness characterized by fever, chills, myalgias, vomiting and some prostation. Symptoms usually start 3 to 10 hours after exposure.
- Aspirated **zinc stearate** may cause severe respiratory irritation.
- PULMONARY EDEMA: Maintain ventilation and oxygenation with close arterial blood gas monitoring. If PO2 remains less than 50 mmHg, PEEP or CPAP may be necessary. Avoid net positive fluid balance; monitor through central line or Swan Ganz catheter.

EYE EXPOSURE

- **Zinc salts** will precipitate eye protein and cause corneal and lens changes.
- DECONTAMINATION: Exposed eyes should be irrigated with copious amounts of tepid water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should probably be seen in a health care facility.
- Rinsing with a 0.05 M neutral sodium edetate may help prevent or reverse a portion of the protein precipitation.
- For all caustic zinc salts an ophthalmic exam is indicated.

DERMAL EXPOSURE

- Irritation caused by **zinc salts** is extremely variable. **Zn oxide** causes little reaction; **zinc dichromate** may cause papulovesicular lesions with exfoliation, and **zinc chloride and phosphide** may cause serious burns.
- DECONTAMINATION: Wash exposed area extremely thoroughly with soap and water. A physician may need to examine the area if irritation or pain persist.

RANGE OF TOXICITY :

- ORAL: A few grams of **zinc chloride** and 10 to 30 g of **zinc sulfate** have been lethal to an adult. **Zinc oxide** has been tolerated in doses of 2 g/kg.

REFERENCE : [Rumack BH & Spoerke DG: POISINDEX(R) Information System. Micromedex Inc., Denver, CO, 1990; CCIS CD-ROM Volume 67, edition exp February, 1991.] **PEER REVIEWED**

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MEDICAL SURVEILLANCE

Frequent exam urine zinc level [Fuscaldo, A., B. J. Erlick, and B. Hindman. (eds.). Laboratory Safety-Theory and Practice. New York: Academic Press, 1980. , p. 268] **PEER REVIEWED**

EDICAL SURVEILLANCE

Medical surveillance shall be made available ... for all persons occupationally exposed to zinc oxide. Preplacement medical examinations shall include comprehensive or interim work history and comprehensive or interim medical history. The examination shall give special emphasis to the respiratory tract. Such tests as chest X-rays and pulmonary function studies may be considered by the responsible physician. [Nat'l Research Council Canada; Zinc Oxide p.2 (1975) NRCC No. 76-104] **PEER REVIEWED**

UMAN TOXICITY EXCERPTS

... TOXICITY OF ZINC CMPD BY MOUTH IS LOW. ... /IT WAS CONCLUDED FROM REVIEW OF LITERATURE ON METAL FUME FEVER & INJURY FROM POWDERS & DUSTS OF ZINC/ THAT SEVERE EXPOSURE TO ZINC MIGHT GIVE RISE TO GASTRITIS, WITH VOMITING, DUE TO SWALLOWING OF DUSTS OF ZINC CMPD. /ZINC CMPD/ [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: , p. 645] **PEER REVIEWED**

UMAN TOXICITY EXCERPTS

Metal fume fever (zinc chills, brass founder's ague, etc) may result from the inhalation of zinc oxide fume. The symptoms include fever, chills, muscular pain, nausea and vomiting ... can also result from breathing finely divided zinc oxide dust. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: , p. 645] **PEER REVIEWED**

AN TOXICITY EXCERPTS

... /IT IS REPORTED/ THAT IF MEN WORK IN UNCONTROLLED LEVELS OF FUMES OR DUST OF ZINC OXIDE ... THEY DEVELOP DERMATITIS, BOILS, CONJUNCTIVITIS, & GI DISTURBANCES. IN THIS REPORT SUCH FINDINGS DO NOT OCCUR UNTIL EXPOSURE HAS LASTED MORE THAN 6 MO. [Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. , p. 187] **PEER REVIEWED**

UMAN TOXICITY EXCERPTS

INHALATION OF AIR CONTAINING ZINC OXIDE AT 1-34 MG/CU M CAUSES METAL FUME FEVER & PNEUMONITIS ... . [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 74] **PEER REVIEWED**

JMAN TOXICITY EXCERPTS

... TWO VOLUNTEERS /WERE EXPOSED/ TO AIR CONCN OF 600 MG ZN/CU M (AS ZINC OXIDE) MODERATE SYMPTOMS WITH TYPICAL FEBRILE REACTION & LEUKOCYTOSIS WERE RECORDED AFTER 10.5 & 12 MIN EXPOSURE. [Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. , p. 674] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

... /DISTINCTION IS MADE/ BETWEEN EFFECTS OF ZINC OXIDE POWDER, WHICH HAS PRODUCED RELATIVELY LITTLE SYSTEMIC DISTURBANCE, & FUMES OF FRESHLY BURNED ZINC OXIDE, WHICH ... /IS REGARDED/ AS SPECIFIC TO INCIDENCE OF CHILLS & FEVER. [Browning, E. Toxicity of Industrial Metals. 2nd ed. New York:

Appleton-Century-Crofts, 1969. , p. 352] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

Clinically latent liver dysfunction has been reported in 15 of 25 workers exposed at high levels of zinc oxide (50 mg/cu m) as evidenced by abnormal levels in liver function tests. ... Radiological evidence of peptic ulcer, found in three elevated uropepsin levels was felt to be indicative of toxic damage to the GI tract. ... Although zinc oxide is a constituent of many topical dermatologic preparations and has demomstrated low potential for skin irritation, nevertheless it was reported in 1921 that 14 of 17 men employed in making zinc oxide had experienced an occupational dermatitis, "oxide pox." The eruptions, which were small, red, hard, projecting papules with a white central plug, usually persisted for a wk or 10 days. In 13 of the cases, the pubic region, scrotum, and inner aspects of the thighs were involved, and in 4 cases, the axilla and inner surfaces of the arms as well. /It was/ ... concluded that zinc oxide had combined with debris and bacteria to block sebaceous glands as a result of lack of personal hygiene. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2047] **PEER REVIEWED**

UMAN TOXICITY EXCERPTS

HEMOLYTIC REACTIONS, ADSORPTION TESTS, & MICROSCOPIC EVIDENCE PROVIDED INFORMATION ABOUT THE INTERACTIONS BETWEEN EITHER ZINC, ZINC OXIDE, OR ZINC SULFIDE DUST PARTICLES & HUMAN RED BLOOD CELLS. IN VITRO, ZINC DUST EXTENSIVELY HEMOLYZED RED BLOOD CELLS & ABSORBED THE LIBERATED HEMOGLOBIN. METALLIC ZINC HAD THE GREATEST HEMOLYTIC EFFECT & THE LARGEST HEMOGLOBIN BINDING CAPACITY; IT WAS FOLLOWED BY ZINC OXIDE & ZINC SULFIDE. [DELBECK G, DELBECK M; RES EXP MED 160 (4): 255-60 (1973)] **PEER REVIEWED**

JMAN TOXICITY EXCERPTS

The ingestion of this cmpd produces intense gastroenteritis, since severe irritation and even corrosion of the mucosa of the stomach follow the formation of zinc chloride in the stomach by the interaction of zinc oxide and the hydrochloric acid of the gastric juice. [Arena, J.M. and Drew, R.H. (eds.) Poisoning-Toxicology, Symptoms, Treatments. 5th ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. 350] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

INHALATION OF FUMES OF ZINC OXIDE RESULTS IN A MALARIA LIKE ILLNESS WITH ONSET SOME HOURS AFTER EXPOSURE. ... THE SYMPTOMS INCLUDE CHILLS AND FEVER, ... NAUSEA, AND SOMETIMES VOMITING, DRYNESS OF THE THROAT, COUGH, FATIGUE, YAWNING, WEAKNESS, AND ACHING OF THE HEAD AND BODY. ... THE CONDITION LASTS A DAY AND IS NEVER FATAL. ... WORKERS ARE MORE SUSCEPTIBLE ON MONDAYS, AND ON WEEK DAYS FOLLOWING A HOLIDAY, THAN ON OTHER WORKDAYS. ... [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1188] **PEER REVIEWED**

F'JMAN TOXICITY EXCERPTS

CHRONIC ZINC POISONING FROM DUST OR FUME IS QUESTIONABLE. ...

/DATA/ INDICATE THAT RELATIVELY LARGE AMT OF ZINC MAY PASS FOR YEARS THROUGH KIDNEYS & GASTROINTESTINAL TRACT WITHOUT CAUSING ANY DETECTABLE CLINICAL DAMAGE. /ZINC CMPD/ [Browning, E. Toxicity of Industrial Metals. 2nd ed. New York: Appleton-Century-Crofts, 1969. , p. 353] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

... /IT WAS/ CONCLUDED THAT ... ABNORMAL AMT OF ZINC MAY ENTER & LEAVE THE BODY FOR YEARS WITHOUT CAUSING SYMPTOMS OR EVIDENCE WHICH CAN BE DETECTED CLINICALLY OR BY LABORATORY EXAMINATIONS OF GASTROINTESTINAL, KIDNEY, OR OTHER DAMAGE ... /ZINC/ [Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. , p. 187] **PEER REVIEWED**

UMAN TOXICITY EXCERPTS

SINCE ZINC IS NORMAL & NECESSARY IN HUMAN METABOLISM, THERE IS LESS LIKELIHOOD OF OCCUPATIONAL POISONING. WHEN POISONING DOES OCCUR, IT IS ALMOST ALWAYS CAUSED BY HEAVY EXPOSURE TO ZINC OXIDE POWDER ... [Hamilton, A., and H. L. Hardy. Industrial Toxicology. 3rd ed. Acton, Mass.: Publishing Sciences Group, Inc., 1974. , p. 187] **PEER REVIEWED**

UMAN TOXICITY EXCERPTS

ZINC SALTS ARE RELATIVELY NONTOXIC OWING TO EFFICIENT ZINC HOMEOSTATIC MECHANISM ... /ZINC SALTS/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 72] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

Of several effects resulting from industrial exposure to zinc, that of zinc fume fever from freshly formed zinc oxide fume ... /is/ most commonly described & best documented. In survey of 102 brass foundry workers, 20% had attacks of "brass foundryman's ague" on avg of once/wk, 13% once/mo, 17% once/yr, 11% twice/wk, 14% twice/mo, 6% twice/yr, 2% 3 times/mo, 1% 3 times/yr & about 10% 4 times/yr. The attacks among 88% of workers occurred only during winter mo when ventilation was inadequate, but 12% had attacks regardless of season. ... Zinc oxide level that caused the attacks /was not determined/. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2045] **PEER REVIEWED**

ON-HUMAN TOXICITY EXCERPTS

... /GUINEA PIGS EXPOSURE/ OF AN HR TO CONCN OF ... 1000 TO 2600 MG/CU M RESULTED IN INITIAL DROP IN BODY TEMP OF 0.5 TO 2 DEG, FOLLOWED 6 TO 18 HR LATER BY A RISE TO 0.5 TO 1 DEG C ABOVE NORMAL. ANIMALS EXPOSED AT CONCN UP TO 2500 MG/CU M FOR 3 TO 4 HR DIED DURING OR IMMEDIATELY AFTER EXPOSURE. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: , p. 645] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

RABBITS, RATS & CATS EXPOSED FOR 3.5 HR TO ZINC OXIDE FUMES AT CONCN OF 110-600 MG/CU M REACTED WITH TRANSIENT FALL IN BODY TEMP FOLLOWED BY MARKED LEUKOCYTOSIS. IN HEAVILY EXPOSED ANIMALS AUTOPSY STUDIES SHOWED SIGNS OF BRONCHOPNEUMONIA. [Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds).

Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. V2 671] **PEER REVIEWED**

ON-HUMAN TOXICITY EXCERPTS

LONG-TERM EXPOSURE OF ZINC OXIDE (ZNO) TO RATS AT CONCN OF 15 MG/CU M FOR 8 HR DAILY UP TO 84 DAYS GAVE RISE TO MINOR MICROSCOPICAL CHANGES WITH SIGNS OF CHRONIC INFLAMMATION & SLIGHT CHANGES IN 2 OF 10 PULMONARY FUNCTION TESTS STUDIED. [Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. V2 671] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

ZINC OXIDE ... /IN DIET OF RATS AT 0.5% DOES/ NOT RETARD GROWTH ... /BUT DOES/ RETARD GROWTH WHEN DIET CONTAINS 1% ZINC. ... IN PREGNANT RATS, DIETARY ZINC OXIDE AT 4000 PPM ZINC CAUSES RESORPTION & DEATH OF FETUSES. [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 72] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

... 175 TO 1000 MG OF ZINC OXIDE/DAY /WERE GIVEN/ FOR PERIODS OF ... 3 TO 53 WK TO DOGS & CATS, & ... WAS TOLERATED; GLYCOSURIA OCCURRED IN DOGS, & FIBROUS DEGENERATION OF PANCREAS IN SOME OF CATS ... NO MANIFEST INJURY OCCURRED IN RATS FROM ADMIN OF 0.5 TO 34.4 MG ZNO/DAY FOR PERIODS OF 1 MO TO 1 YR. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2040] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

FIRST SYMPTOMS OF CHRONIC POISONING IN PIGS ARE DEPRESSED RATE OF GAIN, REDUCED APPETITE & REDUCED EFFICIENCY OF FOOD CONVERSION. IN ADDN, ARTHRITIS, EXTERNAL HEMORRHAGE IN AXILLARY SPACES, GASTRITIS, CATARRHAL ENTERITIS, CONGESTION OF MESENTERY & HEMORRHAGES IN VENTRICLES OF BRAIN, LYMPH NODES & SPLEEN HAVE BEEN DESCRIBED. [Clarke, E.G., and M. L. Clarke. Veterinary Toxicology. Baltimore, Maryland: The Williams and Wilkins Company, 1975. , p. 106] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

... ZINC OXIDE FUMES FROM WELDING OF GALVANIZED MATERIALS ARE ... /THOUGHT/ TO BE RESPONSIBLE FOR POISONING OF CATTLE IN VICINITY OF WELDING OPERATIONS. ... [Clarke, M. L., D. G. Harvey and D. J. Humphreys. Veterinary Toxicology. 2nd ed. London: Bailliere Tindall, 1981. , p. 76] **PEER REVIEWED**

N ON-HUMAN TOXICITY EXCERPTS

Poisoning with zinc oxide fumes ... give rise to fever, dyspnea, anorexia, suppression of milk yield, & subcutaneous emphysema of neck & chest. These signs are followed by ... recovery in few days or death. Characteristic lesions are interstitial pulmonary emphysema & atelectasis, believed to be due to a form of anaphylactic shock. /Zinc oxide fume/ [Clarke, M. L., D. G. Harvey and D. J. Humphreys. Veterinary Toxicology. 2nd ed. London: Bailliere Tindall, 1981. , p. 77] **PEER REVIEWED**

N N-HUMAN TOXICITY EXCERPTS

... Zinc oxide /given/ to sheep in food at concn exceeding 1000 mg/kg recorded poor growth, microcytic and hypochromic anemia after several wk of exposure. Similar signs of chronic toxicity from high dietary zinc intake have been found in horses. ... [Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. V2 673] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

SYMPTOMS OF ZINC (ZN) TOXICITY ARE LASSITUDE, SLOWER TENDON REFLEXES, BLOODY ENTERITIS, DIARRHEA, LOWERED LEUKOCYTE COUNT AND DEPRESSION OF CNS ... AND PARALYSIS OF EXTREMITIES. /ZN CMPD/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 72] **PEER REVIEWED**

ABSORPTION, DISTRIBUTION AND EXCRETION

URINARY & BLOOD EXAM /IN WORKERS IN MFR OF ZINC OXIDE & OTHER CMPD/ INDICATED THAT ZINC WAS ABSORBED & EXCRETED IN AMT HIGHER THAN NORMAL, FROM 0.12-3.93 MG/100 CC IN URINE (NORMAL AVG ... EST AS 1.06 MG); FECAL ZN WAS ALSO HIGH, BUT THIS REPRESENTED TO CONSIDERABLE EXTENT ZN SWALLOWED & PASSED THROUGH GI TRACT UNABSORBED. [Browning, E. Toxicity of Industrial Metals. 2nd ed. New York: Appleton-Century-Crofts, 1969. , p. 353] **PEER REVIEWED**

BSORPTION, DISTRIBUTION AND EXCRETION

... THESE FIGURES, /0.12 TO 3.93 MG/100 CC URINE/ INDICATE THAT RELATIVELY LARGE AMT OF ZINC MAY PASS FOR YEARS THROUGH KIDNEYS & GI TRACT WITHOUT CAUSING ANY DETECTABLE CLINICAL DAMAGE. /ZINC CMPD/ [Browning, E. Toxicity of Industrial Metals. 2nd ed. New York: Appleton-Century-Crofts, 1969. , p. 353] **PEER REVIEWED**

BSORPTION, DISTRIBUTION AND EXCRETION

CONCN OF 0.6 TO 0.7 MG/L HAVE BEEN FOUND IN URINE OF WORKERS EXPOSED TO ZINC OXIDE IN CONCN BETWEEN 3 & 5 MG/CU M. THESE VALUES ARE NOT EXCESSIVELY ELEVATED COMPARED TO NORMAL VALUES. [Friberg, L., G.R. Nordberg, and V.B. Vouk. Handbook on the Toxicology of Metals. New York: Elsevier North Holland, 1979. , p. 680] **PEER REVIEWED**

..BSORPTION, DISTRIBUTION AND EXCRETION

The gastrointestinal absorption of soluble zinc salts in mammals is highly variable; it averages about 50% of the dietary intake and is dependent upon the zinc level in the diet. ... When small amounts of zinc are fed to experimental animals and ruminants, the absorption of zinc may increase to 80% ... . /Zinc cmpd/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 70] **PEER REVIEWED**

; BSORPTION, DISTRIBUTION AND EXCRETION

ZINC CAN BIND READILY TO SULFHYDRYL GROUPS, AMINO GROUPS & IMIDAZOLE GROUPS OF PROTEINS, AMINO ACIDS & OTHER ORGANIC MOLECULES. ... ABSORBED PRIMARILY FROM DUODENUM. IT BINDS TO ALL PROTEINS OF PLASMA ... MOST LOOSELY BOUND TO ALBUMIN & THIS MAY BE IMPORTANT FOR TRANSPORT TO & FROM TISSUES. /ZINC ION/ [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack

Publishing Co., 1975. , p. 970] **PEER REVIEWED**

ABSORPTION, DISTRIBUTION AND EXCRETION

The highest concn /of zinc/ appears in the choroid of the eye, spermatozoa, hair, nails. ... In plasma, most zinc is protein bound, predominately to albumin, alpha 2-macroglobulin, and transferrin. /Zinc ion/ [American Medical Association, Department of Drugs. Drug Evaluations. 6th ed. Chicago, Ill: American Medical Association, 1986. , p. 859] **PEER REVIEWED**

ABSORPTION, DISTRIBUTION AND EXCRETION

ZINC CONCN IN GASTRIC CONTENT, BLOOD, LIVER, KIDNEY, & MUSCLES OF SUICIDAL VICTIM WERE 22.8, 2.4, 5.3, 5.3, & 5.7 MG/100 G, RESPECTIVELY, VERSUS CORRESPONDING NORMAL LEVELS OF 1.9, 1.5, 8.0, 4.0, & 5.0 MG/100 G. /ZINC/ [GIEBELMANN R ET AL; DEUT GESUNDHEITSW 29 (29): 1378-9 (1974)] **PEER REVIEWED**

..BSORPTION, DISTRIBUTION AND EXCRETION

ABSORPTION BY GI TRACT IS VARIABLE IN ANIMALS ... & POOR IN HUMAN ... EXCRETION IS CHIEFLY BY FECES, IN AMT ROUGHLY EQUAL TO THAT ADMIN ... URINARY EXCRETION IS SMALL ... DOES NOT VARY WITH INTAKE & IS INDEPENDENT OF URINE VOLUME ... /ZINC/ [Browning, E. Toxicity of Industrial Metals. 2nd ed. New York: Appleton-Century-Crofts, 1969. , p. 349] **PEER REVIEWED**

mECHANISM OF ACTION

METAL FUME FEVER HAS BEEN ASSOCIATED WITH INHALATION OF ZINC OXIDE FUMES ... THE PATHOGENESIS OF SYNDROME IS NOT CLEAR, BUT SEVERAL INDICATIONS OF AN ALLERGIC BACKGROUND HAVE COME FORTH. IT HAS BEEN PROPOSED THAT ZINC ENTERS BLOOD CIRCULATION & FORMS A SENSITIZING COMPLEX WITH PLASMA PROTEINS. /METAL FUME FEVER/ [Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. , p. 673] **PEER REVIEWED**

..ECHANISM OF ACTION

The ingestion of this cmpd produces intense gastroenteritis, since severe irritation and even corrosion of the mucosa of the stomach follow the formation of zinc chloride in the stomach by the interaction of zinc oxide and the hydrochloric acid of the gastric juice. [Arena, J.M. and Drew, R.H. (eds.) Poisoning-Toxicology, Symptoms, Treatments. 5th ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. 350] **PEER REVIEWED**

] ECHANISM OF ACTION

... Freshly formed fumes are ... composed of ... particles in range of 0.05 to 0.5 um, & ... /have/ increased activity when they come into contact with the alveolar walls of lung. As fumes age they become less reactive because they tend to agglomerate or form aggregates & settle out of atmosphere ... thereby reducing concn of reactive particluates in lung. ... The size of particles is important factor in producing the illness. ... Finely divided particles of metals /are/ so small that they behave much like a gas & act on the alveolar surfaces, affecting the lung tissue & not upper respiratory tract. /Zinc/ [International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. , p. 1339] **PEER REVIEWED**

NTERACTIONS

LONG TERM PRESCRIPTION OF ZINC MAY ... IN CERTAIN PATIENTS PRODUCE A SECONDARY COPPER DEFICIENCY AS MANIFESTED BY HYPOCHROMIC MACROCYTIC ANEMIA. THE MECHANISM ... IS PROBABLY COMPETITION BETWEEN ZINC & COPPER AT ABSORPTION SITES IN THE GUT. /ZINC SALTS/ [Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. V2 675] **PEER REVIEWED**

INTERACTIONS

The presence of zinc oxide inhibits the therapeutic effects of 8-hydroxyquinoline in ointments. [Stockley, I.H. Drug Interactions. Boston: Blackwell Scientific Publications, 1981. , p. 90] **PEER REVIEWED**

IONECESSITY

ZINC DEFICIENCY DECREASES PRODUCTION OF DNA & RNA, WHICH LEADS TO REDUCED PROTEIN SYNTHESIS. ... ZINC DEFICIENT DIETS ... SHOWED THAT GROWTH ARREST OCCURRED AMONG RATS FED WITH FOOD CONTAINING SLIGHTLY LESS THAN 12 MG/KG OF ZINC. TYPICAL SIGNS OF SEVERE DEFICIENCY INCL DERMATITIS, EMACIATION, TESTICULAR ATROPHY, RETARDED GROWTH & ANOREXIA. ... ENDEMIC ZINC DEFICIENCY SYNDROME AMONG YOUNG MEN & WOMEN HAS BEEN REPORTED FROM IRAN & EGYPT. PROMINENT FEATURES WERE RETARDED GROWTH, INFANTILE TESTIS, DELAYED SEXUAL MATURATION, ANEMIA, HEPATOSPLENOMEGALY & HYPERPIGMENTATION. /ZINC CMPD/ [Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. V2 668] **PEER REVIEWED**

BIONECESSITY

ZINC IS OMNIPRESENT IN LIVING ORGANISMS & RANKS WITH MOST ABUNDANT OF TRACE METALS IN MAN. AS FAR AS IS KNOWN, ALL LIVING THINGS REQUIRE ZINC, & IT IS CONSTITUENT OF ALL CELLS SERVING AS COFACTOR IN MANY ESSENTIAL ENZYME SYSTEMS. /ZINC/ [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2041] **PEER REVIEWED**

IONECESSITY

ZINC IS UBIQUITOUS & IS CONSIDERED AN ESSENTIAL TRACE ELEMENT. ITS NECESSARY ROLES INVOLVE ENZYMES & ENZYMATIC FUNCTIONS, PROTEIN SYNTHESIS, & CARBOHYDRATE METABOLISM. IT IS NECESSARY FOR NORMAL GROWTH & DEVELOPMENT IN MAMMALS & BIRDS. HUMAN DWARFISM & LACK OF SEXUAL DEVELOPMENT HAVE BEEN RELATED TO ZINC DEFICIENCY. ZINC IS PRESENT IN ... METALLOENZYMES INCL CARBONIC ANHYDRASE, CARBOXYPEPTIDASE, ALCOHOL DEHYDROGENASE, GLUTAMIC DEHYDROGENASE, LACTIC DEHYDROGENASE & ALKALINE PHOSPHATASE. /ZINC CMPD/ [Doull, J., C.D. Klaassen, and M. D. Amdur (eds.). Casarett and Doull's Toxicology. 2nd ed. New York: Macmillan Publishing Co., 1980. , p. 460] **PEER REVIEWED**

BIONECESSITY

Zinc deficiency in the new born may be manifested by dermatitis, loss of hair, impaired healing, susceptibility to infections, and neuropsychologic abnormalities. ... Less common zinc deficiency may occur with myocardial infarction, arthritis, and even hypertension. /Zinc ion/ [Doull, J.,

C.D.Klassen, and M.D. Amdur (eds.). Casarett and Doull's Toxicology. 3rd ed., New York: Macmillan Co., Inc., 1986. , p. 618] **PEER REVIEWED**

IONECESSITY

... Zinc is a membrane stabilizer and a participant in electron transfer processes. Zinc hormone interactions incl hormonal influence on absorption, distribution, transport, and excretion of zinc and zinc influence on synthesis, secretion, receptor binding, and function of numerous hormones. ... Zinc is required for maintenance of normal plasma concn of vitamin A and for normal mobilization of vitamin A from the liver. /Zinc ion/ [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 15(81) 590] **PEER REVIEWED**

IONECESSITY

... Maternal serum zinc levels are significantly lower in those giving birth to anencephalics than in controls. ... Zinc deficiency in pt with acrodermatitis enteropathica might account for two major defects occurring among seven pregnant pt with the disease. The two defects were anencephaly and fatal achondrogenesis. /Zinc ion/ [Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986. , p. 614] **PEER REVIEWED**

IONECESSITY

Rats /were placed/ on a marginally deficient zinc diet and at the onset of gestation placed on a zinc deficient diet. Nearly all of the surviving fetuses exhibited one or more congenital malformations. Cleft palate, skeletal defects, hydrocephalus (65%), eye, heart, lung and urogenital (49%) abnormalities were found. A reduction of zinc content in the fetuses was found. ... After exposing rats to only a few days of zinc deficiency were able to produce fetal defects. ... A reduction in the otoliths of rats fetuses whose mothers were maintained on deficient diets, /was produced/. Evidence that a 3 day period of zinc deficiency can produce abnormal rat blastocytsts and morulae has been published ... . /Zinc ion/ [Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986. , p. 614] **PEER REVIEWED**

IONECESSITY

The daily zinc requirement has been recommended as 15 mg for adults and 25 mg for nursing mothers. /Zinc ion/ [Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. V2 668] **PEER REVIEWED**

BIONECESSITY

... Has many important natural functions in the eye ... . /Zinc ion/ [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. 992] **PEER REVIEWED**

THERAPEUTIC USES

IT HAS MILD ASTRINGENT & ANTISEPTIC ACTION. IT IS USED IN SKIN DISEASES & INFECTIONS SUCH AS ECZEMA, IMPETIGO, RINGWORM, VARICOSE ULCERS, PRURITUS, & PSORIASIS. [Gilman, A.G., L.S.Goodman, and A. Gilman. (eds.). Goodman and Gilman's The

Pharmacological Basis of Therapeutics. 7th ed. New York: Macmillan Publishing Co., Inc., 1985. , p. 967] **PEER REVIEWED**

THERAPEUTIC USES

/ZINC OXIDE PASTE WITH SALICYLIC ACID NF IS FREQUENTLY USED/ IN TREATMENT OF ATHLETE'S FOOT & OTHER DERMATOMYCOSES. PRESENCE OF ZINC OXIDE IMPARTS ASTRINGENT & PROTECTIVE PROPERTY TO THIS PASTE. ASTRINGENT ACTION IS DESIRED TO REDUCE INFLAMMATION & TO CLOSE FISSURES. /ZINC OXIDE PASTE WITH SALICYLIC ACID/ [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975. , p. 719] **PEER REVIEWED**

THERAPEUTIC USES

IT IS ALSO USED IN DENTAL CEMENTS & TEMPORARY FILLINGS. DOSE: TOPICAL, AS 15 TO 25% LOTION, OINTMENT, OR PASTE. [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975. , p. 719] **PEER REVIEWED**

THERAPEUTIC USES

... In some pt dark adaptation improved when zinc was admin; in these pt treatment with vitamin A had failed. ... In a pt who had abnormal dark adaptation associated with Crohn's disease and low serum zinc, there was improvement of the dark adaptation when zinc was admin. [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. 992] **PEER REVIEWED**

THERAPEUTIC USES

Recommended daily intakes during nutritional support: Adult: 1.5-2.5 mg; Pediatric: 100-300 ug/kg (below age 6) [American Medical Association, Department of Drugs. Drug Evaluations. 6th ed. Chicago, Ill: American Medical Association, 1986. , p. 865] **PEER REVIEWED**

DRUG WARNINGS

Incompatible with benzylpenicillin [Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982. , p. 509] **PEER REVIEWED**

DRUG WARNINGS

... Ingestion of excessive doses for prolonged periods is not recommended. High concn alter the immune response. ... Excessive intake also may induce copper and iron deficiency ... and may cause nausea, vomiting, headache, chills, fever, malaise, and abdominal pain. [American Medical Association, Department of Drugs. Drug Evaluations. 6th ed. Chicago, Ill: American Medical Association, 1986. , p. 859] **PEER REVIEWED**

NATURAL OCCURRING SOURCES

ZINC OCCURS IN NATURE ... /AS ZINC OXIDE/. [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 69] **PEER REVIEWED**

ARTIFICIAL SOURCES

... Zinc oxide is produced ... in zinc smelting, manufacture of zinc oxide and powder, production of brass, and melting of galvanized iron. Zinc oxide fumes may also be produced secondary to torch welding and cutting of zinc containing or galvanized materials. [Friberg, L., Nordberg, G.F., Kessler, E.

and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. , p. 667] **PEER REVIEWED**

ENVIRONMENTAL FATE

CONTAMINATION OF PASTURES WITH ZINC OXIDE IS KNOWN TO OCCUR IN VICINITY OF WORKS WHERE ZINC IS PRODUCED FROM ITS ORES & IS LIKELY IN NEIGHBORHOOD OF BRASS FOUNDRIES. [Clarke, E.G., and M. L. Clarke. Veterinary Toxicology. Baltimore, Maryland: The Williams and Wilkins Company, 1975. , p. 104] **PEER REVIEWED**

PROBABLE ROUTES OF HUMAN EXPOSURE

Zinc poisoning is mostly accidential from the intake of pesticides, inadvertant therapeutic use of heavy doses of zinc salts, or drinking of acidic juices or brews made in galvanized iron utensils. /Zinc cmpd/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 69] **PEER REVIEWED**

PROBABLE EXPOSURES

EXPOSURE TO ZINC FUMES, PARTICULARLY ZINC OXIDE, IS POTENTIAL RISK WHEREEVER ZINC OXIDE IS PRODUCT OR BY PRODUCT EG, IN ZINC SMELTING, MFR OF ZINC OXIDE & POWDER, PRODN OF BRASS, & MELTING OF GALVANIZED IRON. [Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. , p. 667] **PEER REVIEWED**

PROBABLE EXPOSURES

... /IT WAS/ CONCLUDED THAT METAL FUME FEVER WOULD NOT RESULT FROM CONCN ... BELOW 15 MG/CU M, & THIS CONCN WAS RECOMMENDED TLV FOR NUMBER OF YEARS. MORE RECENT EXPERIENCE ... /INDICATE CONCN/ IN NON-FERROUS FOUNDRIES ... /PRODUCE/ ZINC CHILLS ... & HAVE BEEN REPORTED BELOW ... 5 MG/CU M. /ZINC CMPD/ [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: , p. 645] **PEER REVIEWED**

ALLOWABLE TOLERANCES

Residues of zinc oxide are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest. [40 CFR 180.1001 (a) (7/1/87)] **PEER REVIEWED**

OSHA STANDARDS

8-hr Time-Weighted avg: (5 mg/cu m) /Zinc oxide fume/ [29 CFR 1910.1000 (7/1/86)] **PEER REVIEWED**

NIOSH RECOMMENDATIONS

10 hr TWA 5 mg/cu m, 15 min ceiling 15 mg/cu m [NIOSH. Pocket Guide to Chemical Hazards. 5th Printing/Revision. DHHS (NIOSH) Publ. No. 85-114. Washington, D.C.: U.S. Dept. of Health and Human Services, , p. 238] **PEER REVIEWED**

THRESHOLD LIMIT VALUES

Time Weighted Avg (TWA) 5 mg/cu m; Short Term Exposure Limit (STEL) 10 mg/cu m (1976) /Fume/ [American Conference of Governmental Industrial Hygienists. Threshold Limit Values and Biological Exposure Indices for 1989-1990. Cincinnati, OH: American , p. 43] **QC REVIEWED**

THRESHOLD LIMIT VALUES

Time Weighted Avg (TWA) 10 mg/cu m; the value is for total dust containing no asbestos & <1% free silica. (1976) /Dust/ [American Conference of Governmental Industrial Hygienists. Threshold Limit Values and Biological Exposure Indices for 1989-1990. Cincinnati, OH: American , p. 43] **QC REVIEWED**

OTHER OCCUPATIONAL PERMISSIBLE LEVELS

Other /mel/ recommendations: USSR (1967), Czechoslovakia (1969), East Germany (1973), West Germany (1974) and Sweden (1975) 5 mg/cu m. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: , p. 645] **PEER REVIEWED**

WATER STANDARDS

Toxic pollutant designated pursuant to section 307(a)(1) of the Clean Water Act and is subject to effluent limitations. /Zinc and compounds/ [40 CFR 401.15 (7/1/87)] **PEER REVIEWED**

WATER STANDARDS

The secondary contaminant level of zinc for public water systems is 5 mg/l. These regulations control contaminants in drinking water that primarily affect the aesthetic qualities relating to the public acceptance of drinking water. The States may establish higher or lower levels which may be appropriate dependent, upon local conditions such as unavailability of alternate source waters or other compelling factors, provided that public health and welfare are not adversely affected. /Soluble zinc salts/ [40 CFR 143 (7/1/87)] **PEER REVIEWED**

WATER STANDARDS

For total recoverable zinc the criterion to protect freshwater aquatic life ... is 47 ng/l as a 24 hr average ... at hardnesses of 50, 100, and 200 mg/l as CaCO3 the concentration of total recoverable zinc should not exceed 180, 320, 570 ug/l at any time. /Soluble zinc salts/ [USEPA/OWRS; Quality Criteria for Water 1986 Zinc (1986) EPA 440/5-86-001] **PEER REVIEWED**

WATER STANDARDS

For total recoverable zinc the criterion to protect saltwater aquatic life ... is 58 ug/l as a 24 hr average and the concentration should not exceed 170 ug/l at any time. /Soluble zinc salts/ [USEPA/OWRS; Quality Criteria for Water 1986 Zinc (1986) EPA 440/5-86-001] **PEER REVIEWED**

FDA REQUIREMENTS

Zinc oxide is generally recognized as safe when used as a dietary supplement in accordance with good manufacturing or feeding practice. [21 CFR 182.5991 (4/1/88)] **PEER REVIEWED**

FDA REQUIREMENTS

Bottled water shall, when a composite of analytical units of equal volume from a sample is examined by the methods described in paragraph (d)(1)(ii) of this section, meet the standards of chemical quality and shall not contain zinc in excess of 5.0 mg/l. /Soluble zinc salts/ [21 CFR 103.35 (4/1/86)] **PEER REVIEWED**

FDA REQUIREMENTS

(a) Product. Zinc oxide. (b) Conditions of use. This substance is generally recognized as safe when used as a nutrient in accordance with good manufacturing practice. [21 CFR 182.8991 (4/1/88)] **PEER REVIEWED**

FDA REQUIREMENTS
The color additive zinc oxide shall conform to the specifications in the CFR 73.1991 and shall be free from impurities other than those named; including zinc oxide (as ZnO) in not less than 99%, to the extent that such impurities may be avoided by manufacturing practice. [21 CFR 73.1991 (4/1/88)] **PEER REVIEWED**

FDA REQUIREMENTS
Zinc oxide may be safely used in cosmetics, including cosmetics intended for use in the area of the eye, in amounts consistent with good manufacturing practice. [21 CFR 73.2991 (4/1/88)] **PEER REVIEWED**

FIFRA REQUIREMENTS
Residues of zinc oxide are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest. [40 CFR 180.1001 (a) (7/1/87)] **PEER REVIEWED**

SAMPLING PROCEDURES
Analyte: zinc; Matrix: air; Sampler: filter (0.8-um cellulose ester membrane); Flow rate: 1-3 l/min; Vol: min: 2 l at 5 mg/cu m, max: 400 l; Stability: stable /Zinc & cmpd, as zinc/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 7030-1] **PEER REVIEWED**

AMPLING PROCEDURES
Analyte: Zinc; Specimen: Blood or tissue; Vol: 10 ml blood, or 1 g tissue; Preservative: Heparin for blood, none for tissue; Controls: collect 3 blood specimens from unexposed workers; Stability: not established /Elements in blood or tissue/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V1 8005-1] **PEER REVIEWED**

SAMPLING PROCEDURES
Analyte: Zinc; Matrix: urine; Vol: 50-200 ml in polyethylene bottle; Preservative: 5 ml conc NITRIC ACID added after collection; Controls: collect at least 3 urine specimens from unexposed workers; Stability: not established. /Total metal in urine/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V1 8310-1] **PEER REVIEWED**

SAMPLING PROCEDURES
Analyte: Zinc oxide; Matrix: air; Sampler: Filter (0.8 um PVC membrane, 25 mm dia); Flow rate: 1-3 l/min; Vol: min: 10 l, max: 400 l; Stability: stable [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH 7502-1] **PEER REVIEWED**

SAMPLING PROCEDURES
Analyte: Mass of respirable dust fraction; Matrix: air; Sampler: Cyclone + filter (10-mm Dorr-Oliver cyclone + tared 5

99.99%, and 99.999%, -325 mesh, 2 micron, luminescent and emissive grade [Kuney, J.H. and J.N. Nullican (eds.) Chemcyclopedia. Washington, DC: American Chemical Society, 1988. , p. 219] **PEER REVIEWED**

FORMULATIONS/PREPARATIONS
Mixed with zinc oxide as "mineral white" [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1458] **PEER REVIEWED**

MANUFACTURERS
Eagle-Picher Industries, Inc, Hq, 580 Walnut St, Cincinnati, OH 45202, (513) 721-7010; Specialty Materials Division; Eagle-Picher Research Laboratory, 200 9th Ave NE, Miami, OK 74354 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1068] **UNREVIEWED**

MANUFACTURERS
General Electric Co, Hq, 3135 Easton Turnpike, Fairfield, CT 06431 (203) 373-2211; Components/Quartz Marketing & Sales Operation, 21800 Tungsten Rd, Cleveland, OH 44117 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1068] **UNREVIEWED**

MANUFACTURERS
GTE Corporation, Hq, One Stamford Forum, Stamford, CT 06904, (203) 357-2000; GTE Products Corp, division; Chemical & Metallurgical Division, Hawes St, Towanda, PA 18848 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1068] **UNREVIEWED**

MANUFACTURERS
Morton Thiokol, Inc, Hq, 110 North Wacker Drive, Chicago, IL 60606, (312) 807-2000; Ventron Division, 150 Andover St, Danvers, MA 01923; CVD Inc, 185 W Boston St, Woburn, MA 01801; Production site: Woburn, MA 01801 [SRI. 1989 Directory of Chemical Producers - United States of America. Menlo Park, CA: SRI International, 1989. , p. 1068] **UNREVIEWED**

OTHER MANUFACTURING INFORMATION
PPTD ZINC SULFIDE OF COMMERCE USUALLY CONTAINS 15-20% WATER OF HYDRATION. THE DRIED PPT MAY HAVE BEEN HEATED TO 725 DEG C IN ABSENCE OF AIR TO OBTAIN SUBSTANTIAL CONVERSION TO WURTZITE, THE FORM PREFERRED BY PIGMENT INDUSTRY. [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1480] **PEER REVIEWED**

MAJOR USES
PIGMENT FOR PAINTS, OILCLOTHS, LINOLEUM, LEATHER, DENTAL RUBBER (ESP IN FORM OF LITHOPONE); MIXED WITH ZINC OXIDE AS "MINERAL WHITE"; ANHYDROUS FORM IS USED IN X-RAY SCREENS & WITH A TRACE OF A RADIUM OR MESOTHORIUM SALT IN LUMINOUS DIALS OF WATCHES; ALSO TELEVISION SCREENS [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1458] **PEER REVIEWED**

MAJOR USES
WHITE & OPAQUE GLASS; BASE FOR COLOR LAKES; PLASTICS; DYEING (HYDROSULFITE PROCESS); FUNGICIDE [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987., p. 1257] **PEER REVIEWED**

MAJOR USES
GREATEST USE OF ZINC SULFIDE IS IN MAKING LITHOPONE PIGMENT

(28% ZNS & 72% BASO4) WHICH IS USED IN PAINT, LINOLEUM & ARTIFICIAL LEATHER ... PHOSPHOR IN X-RAY & TELEVISION SCREENS, & IN LUMINOUS WATCH FACES. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2038] **PEER REVIEWED**

AJOR USES
PIGMENT, EG, FOR PAINTS, INKS, LACQUERS, & COSMETICS [SRI] **PEER REVIEWED**

"AJOR USES
SEMICONDUCTOR [SRI] **PEER REVIEWED**

MAJOR USES
PHOTOCONDUCTOR, EG, FOR SOLAR CELLS [SRI] **PEER REVIEWED**

AJOR USES
Infrared thin film and transmitting devices [Kuney, J.H. and J.N. Nullican (eds.) Chemcyclopedia. Washington, DC: American Chemical Society, 1988. , p. 219] **PEER REVIEWED**

AJOR USES
Use in detinning [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 23(83) 39] **PEER REVIEWED**

..AJOR USES
Component of sulfide flotation concentrates as surfactant to reduce moisture content of coal & iron ore [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. S(84) 318] **PEER REVIEWED**

"AJOR USES
In hydrogen sulfide synthesis [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 22(83) 118] **PEER REVIEWED**

AJOR USES
In optical filter coating [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 16(81) 529] **PEER REVIEWED**

AJOR USES
Use as pigment in paper [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 16(81) 777 s] **PEER REVIEWED**

..AJOR USES
Produce elemental zinc by pressure-leaching zinc sulfide concentrates [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 22(83) 283] **PEER REVIEWED**

"AJOR USES
Zinc, one of the most widely used micronutrients, is applied as sulfates (both basic and normal hydrates), carbonate, sulfide, phosphate, oxide, chelates, and other organic materials. [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984. 10(80) 82] **PEER REVIEWED**

U S. PRODUCTION
(1978) 1.82X10+9 GRAMS (LITHOPONE) [SRI] **PEER REVIEWED**

U.S. IMPORTS
(1979) 7.42X10+8 GRAMS [SRI] **PEER REVIEWED**

U S. IMPORTS

(1981) 6.61X10+8 GRAMS [SRI] **PEER REVIEWED**

COLOR/FORM	EXISTS IN TWO CRYSTALLINE FORMS, ALPHA (WURTZITE) & BETA (SPHALERITE) [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1257] **PEER REVIEWED**
COLOR/FORM	Colorless hexagonal crystals /Alpha/ [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**
COLOR/FORM	Colorless cubic crystals /Beta/ [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**
COLOR/FORM	WHITE TO GRAYISH-WHITE OR YELLOWISH POWDER COLORLESS CUBIC CRYSTALS [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1458] **PEER REVIEWED**
BOILING POINT	1185 deg C at 1 atm [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**
MELTING POINT	1700 +/- 20 deg C at 50 atm /Alpha/ [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**
MOLECULAR WEIGHT	97.45 [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1458] **PEER REVIEWED**
DENSITY/SPECIFIC GRAVITY	3.98 /Alpha/; 4.102 at 25 deg C /Beta/ [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**
SOLUBILITIES	INSOL IN ALKALIES; SOL IN DIL MINERAL ACIDS [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983., p. 1458] **PEER REVIEWED**
SOLUBILITIES	0.00069 g/100 cc water at 18 deg C /Alpha/ [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**
SOLUBILITIES	0.00065 g/100 cc water at 18 deg C /Beta/ [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**
SPECTRAL PROPERTIES	INDEX OF REFRACTION: 2.356, 2.378 /ALPHA/ [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**
SPECTRAL PROPERTIES	INDEX OF REFRACTION: 2.368 /BETA/ [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**
OTHER CHEMICAL/PHYSICAL PROPERTIES	SPECIFIC GRAVITY: 3.98; MP: 1049 DEG C /MONOHYDRATE/ [Weast, R.C. (ed.) Handbook

of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**

OTHER CHEMICAL/PHYSICAL PROPERTIES: BETA FORM CHANGES TO ALPHA FORM AT 1020 DEG C; SUBLIMES AT 1180 DEG C /BETA/ [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1257] **PEER REVIEWED**

OTHER CHEMICAL/PHYSICAL PROPERTIES: YELLOWISH-WHITE POWDER /MONOHYDRATE/ [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**

OTHER CHEMICAL/PHYSICAL PROPERTIES: DEPENDING ON IRON (FE) CONTENT, NATURAL SPECIMENS RANGE IN COLOR FROM LIGHT TAN TO BLACK /ZINC SULFIDE MINERAL/ [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2033] **PEER REVIEWED**

OTHER CHEMICAL/PHYSICAL PROPERTIES: INSOL IN WATER; SOL IN ACIDS /MONOHYDRATE/ [Weast, R.C. (ed.) Handbook of Chemistry and Physics, 68th ed. Boca Raton, Florida: CRC Press Inc., 1987-1988. B-145] **PEER REVIEWED**

OTHER PREVENTIVE MEASURES

In all cases where zinc is heated to the point where fume is produced, it is most important to ensure that adequate ventilation is provided. Individual protection is best ensured by education of the worker concerning metal-fume fever & the provision of local exhaust ventilation, or, in some situations by wearing of supplied-air hood or mask. /Zinc compounds/ [International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. , p. 2342] **PEER REVIEWED**

OTHER PREVENTIVE MEASURES

The most radical measure to be taken ... is the rationalization of the production process: replacement of batch processes by continuous ones, automation, remote control, choice of processes offering conditions of good occupational hygiene, mechanization of manual tasks and transport of the products in tightly closed vessels, and gas-tight enclosure of plant. Sources of release of gases into the air must be enclosed and equipped with exhaust systems. Air containing toxic substances must be cleaned or treated by catalytic after burning before it is discharged into the atmosphere. ... Regular checks for leaks in tight plant, pipework and storage tanks ... are very important. ... Piping and ventilation ductwork ... /should/ resist oxidizers. ... When production is associated with the spread of dust, it is particularly important to use water sprays for dust control. /Oxidizing substances/ [International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. , p. 1576] **PEER REVIEWED**

SHIPMENT METHODS AND REGULATIONS

Whenever hazardous materials are to be transported, Title 49 CFR, Transportation, Parts 100-180, published by the US Dept of Transportation, contain the regulatory requirements and must be consulted. [52 FR 16482 (5/5/87)] **PEER REVIEWED**

DISPOSAL METHODS

SRP: At the time of review, criteria for land treatment or burial (sanitary landfill) disposal practices are subject to significant revision. Prior to implementing land disposal of waste residue (including waste sludge), consult with environmental regulatory agencies for guidance on acceptable disposal practices. [CITATION] **PEER REVIEWED**

DISPOSAL METHODS

Chemical Treatability of Zinc; Concentration Process: Chemical precipitation; Chemical Classification: Metals; Scale of Study: Literature review; Type of Wastewater Used: Unknown; Results of Study: 10.6% reduction by sedimentation. /Zinc compounds/ [USEPA; Management of Hazardous Waste Leachate, EPA Contract No. 68-03-2766 p.E-75 (1982)] **PEER REVIEWED**

DISPOSAL METHODS

Chemical Treatability of Zinc; Concentration Process: Reverse osmosis; Chemical Classification: Metals; Scale of Study: Batch flow; Type of Wastewater Used: Pure compound (one solute in a solvent); Results of Study: 96.6% reduction with C/PEI membrane at pH= 8.0 100% recution with C/PEI membrane at pH= 11.0; CA membrane operated at 400 psig and 16-22 deg C. /Zinc compounds/ [USEPA; Management of Hazardous Waste Leachate, EPA Contract No. 68-03-2766 p.E-88 (1982)] **PEER REVIEWED**

POSAL METHODS

Chemical Treatability of Zinc; Concentration Process: Reverse osmosis; Chemical Classification: Metals; Scale of Study: Batch flow; Type of Wastewater Used: Pure compound (one solute in a solvent); Results of Study: 96.9%-99.5% reduction with CA membrane; CA membrane operated at 400 psig and 16-22% deg C. /Zinc compounds/ [USEPA; Management of Hazardous Waste Leachate, EPA Contract No. 68-03-2766 p.E-88 (1982)] **PEER REVIEWED**

DISPOSAL METHODS

The proprietary Sulfex process (Permutit Co) has been applied to zinc wastes. The process involves addition of ferrous sulfide, which gradually releases sulfide to precipitate the zinc ... . /Zinc/ [Patterson JW; Industrial Wastewater Treatment Technolgy 2nd Edition p.444 (1985)] **PEER REVIEWED**

ISPOSAL METHODS

In the case where zinc removal is the only consideration and recovery is not warranted, removal by precipitation can be accomplished by standard pH adjustment through lime addition, precipitation and flocculation, and sedimentation, employing standard waste treatment equipment. Operating data for existing chemical precipitation units indicate that levels of 1 mg/l or less of zinc are readily obtainable with lime precipitation, although assurance of consistent removal of precipitated zinc to lower levels from the effluent stream may require filtration. /Zinc/ [Patterson JW: Industrial Wastewater Treatment Technology 2nd Edition p.447 (1985)] **PEER REVIEWED**

BILITY/SHELF LIFE

WHEN CONTAINING WATER, IT SLOWLY OXIDIZES IN AIR TO SULFATE

[The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 1458] **PEER REVIEWED**

STABILITY/SHELF LIFE

STABLE IF KEPT DRY [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1257] **PEER REVIEWED**

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NOTE: THE FOLLOWING DOES NOT REFER SPECIFICALLY TO ZINC SULFIDE, BUT IT IS A GENERAL OVERVIEW ON TXOICITY AND FIRST AID FOR SULFIDE EXPOSURE.

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EMERGENCY MEDICAL TREATMENT

o LIFE SUPPORT :

This overview assumes that basic life support measures have been instituted.

CLINICAL EFFECTS :

SUMMARY

- o Hydrogen sulfide is a highly toxic, flammable, colorless gas (TLV(R) = 10.0 ppm) produced by decaying organic matter and has a characteristic odor of rotten egg at low concentrations however, the sense of smell is paralyzed at levels above 50 to 150 ppm.
  1. Exposure to concentrations of 250 ppm causes irritation of mucous membranes, bronchitis and pulmonary edema.
  2. At 500 ppm, symptoms include headache, nausea, weakness, disorientation and coma.
  3. Exposure to higher concentrations can result in immediate death. The mortality rate is in the range of 6%. Characteristic of exposure is the rapid knock down of patients exposed.
  4. Other findings include respiratory depression, tremors, blurred vision, cyanosis, convulsions, and tachycardia.

VITAL SIGNS

- o Patients may present with bradycardia, tachycardia, hyperventilation, respiratory depression even to the point of apnea, and/or hypo-/hypertension.

HEENT

- o Injection of the conjunctivae, seeing colored halos, ocular pain, and blepharospasm may be noted following exposure to 150 to 300 ppm.

CARDIOVASCULAR

- o Tachycardia, bradycardia, cardiac arrhythmias, and hypotension may be noted.

RESPIRATORY

- o Respiratory depression, cyanosis, and dyspnea may be noted following exposure to non-fatal concentrations.

- Exposure to high concentrations will result in rapid respiratory paralysis leading to sudden collapse.

NEUROLOGIC

- Convulsions, coma, and death associated with rapid respiratory paralysis may be noted following exposure to high concentrations.
- Headache, sweating, vertigo, irritability, somnolence, weakness, confusion, and delirium may be noted following exposure to non-fatal levels.

GASTROINTESTINAL

- Nausea and vomiting may be noted.

ACID-BASE

- Lactic acidosis may be noted in survivors.

DERMATOLOGIC

- Skin exposure may result in severe pain, itching, and erythema. Cyanosis may be noted following severe exposure.

LABORATORY :

- Reliable blood sulfide analysis, if available, should be done immediately.
- Monitor methemoglobin levels if indicated.

TREATMENT OVERVIEW :

INHALATION EXPOSURE

- IMMEDIATELY MOVE PATIENT TO FRESH AIR AND ADMINISTER 100% OXYGEN. PREVENT SELF-EXPOSURE and possible death by wearing a self-contained breathing apparatus to rescue the victim.
- SEIZURES: Administer diazepam IV bolus (DOSE: ADULT: 5 to 10 mg initially which may be repeated every 15 minutes PRN up to 30 mg. CHILD: 0.25 to 0.4 mg/kg/dose up to 10 mg/dose). If seizures cannot be controlled or recur, administer phenytoin or phenobarbital.
- HYPOTENSION: Administer IV fluids and place in Trendelenburg position. If unresponsive to these measures, administer dopamine (2 to 5 mcg/kg/min) or norepinephrine (0.1 to 0.2 mcg/kg/min) and titrate as needed to desired response.
- NITRITE THERAPY: Amyl nitrite by inhalation and IV sodium nitrite (found in Lilly Cyanide Antidote Kit) may be beneficial by forming sulfmethemoglobin, thus removing sulfide from combination in tissue. Do NOT use sodium thiosulfate. The antidotal efficacy of nitrite therapy is controversial but is recommended until further studies are available.
- PULMONARY EDEMA: Maintain ventilation and oxygenation with close arterial blood gas monitoring. If PO2 remains less than 50 mmHg, PEEP or CPAP may be necessary. Avoid net positive fluid balance; monitor through central line or Swan-Ganz catheter.

RANGE OF TOXICITY :

- At 0.1 ppm hydrogen sulfide produces a characteristic

rotten egg odor. At 50 to 150 ppm the sense of smell is paralyzed after a short time and gradually worsening symptoms are noted.

- Exposure to greater than 500 ppm results in severe toxicity and death. Respiratory paralysis and death may be noted within 30 to 60 minutes.

TM0092)

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o REFERENCE : [Rumack BH & Spoerke DG: POISINDEX(R) Information System. Micromedex Inc., Denver, CO, 1990; CCIS CD-ROM Volume 67, edition exp February, 1991.] **PEER REVIEWED**

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HUMAN TOXICITY EXCERPTS

ZINC SULFIDE, AS WELL AS BARIUM SULFATE WHICH WAS SIMILARLY ENCOUNTERED /FROM LIQ CENTER OF GOLF BALL ACCIDENTLY SQUIRTED INTO EYE OF 2 CHILDREN/, PRODUCED ONLY SLIGHT MACROPHAGE REACTION & NEGLIBLE TISSUE DAMAGE. [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. 991] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

IF FREE GASTRIC ACIDITY IS HIGH, THE INGESTION OF THESE SALTS MAY RESULT IN THEIR DECOMP TO HYDROGEN SULFIDE IN STOMACH, WITH SUBSEQUENT SYSTEMIC POISONING. /SULFIDE SALTS/ [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. II-116] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

HEMOLYTIC REACTIONS, ADSORPTION TESTS, & MICROSCOPIC EVIDENCE PROVIDED INFORMATION ABOUT THE INTERACTIONS BETWEEN EITHER ZINC, ZINC OXIDE, OR ZINC SULFIDE DUST PARTICLES & HUMAN RED BLOOD CELLS. IN VITRO, ZINC DUST EXTENSIVELY HEMOLYZED RED BLOOD CELLS & ABSORBED THE LIBERATED HEMOGLOBIN. METALLIC ZINC HAD THE GREATEST HEMOLYTIC EFFECT & THE LARGEST HEMOGLOBIN BINDING CAPACITY; IT WAS FOLLOWED BY ZINC OXIDE & ZINC SULFIDE. [DELBECK G, DELBECK M; RES EXP MED 160 (4): 255-60 (1973)] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

Since the 1960's, formerly caustic content /of golf balls/ appears to have been replaced by a non-caustic paste containing barium sulfate, with or without zinc sulfide. Since the 1960's this new preparation has been involved in most recorded injuries from incised or disrupted liquid center golf balls. When the paste is suddenly ejected under great pressure, it can penetrate through the conjunctiva, or into the skin of the eyelids and, less often, into the cornea. Injection into the conjunctiva and lids can be painless, but characteristically a white plaque of injected material is visible beneath the surface. This evokes a non-purulent inflammatory reaction with swelling of the tissue, followed in a few wk by tissue fibrosis. [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. 468] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

TOXICITY OF ZINC CMPD BY MOUTH IS LOW. ... /IT WAS CONCLUDED FROM REVIEW OF LITERATURE ON METAL FUME FEVER & INJURY FROM POWDERS & DUSTS OF ZINC/ THAT SEVERE EXPOSURE TO ZINC MIGHT GIVE RISE TO GASTRITIS, WITH VOMITING, DUE TO SWALLOWING OF DUSTS OF ZINC CMPD. /ZINC CMPD/ [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: , p. 645] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

CHRONIC ZINC POISONING FROM DUST OR FUME IS QUESTIONABLE. ... /DATA/ INDICATE THAT RELATIVELY LARGE AMT OF ZINC MAY PASS FOR YEARS THROUGH KIDNEYS & GASTROINTESTINAL TRACT WITHOUT CAUSING ANY DETECTABLE CLINICAL DAMAGE. /ZINC CMPD/ [Browning, E. Toxicity of Industrial Metals. 2nd ed. New York: Appleton-Century-Crofts, 1969. , p. 353] **PEER REVIEWED**

UMAN TOXICITY EXCERPTS

... TAKEN BY MOUTH ARE RELATIVELY NON-TOXIC, THOUGH THE SOLUBLE SALTS IN LARGE DOSES MAY CAUSE VOMITING & DIARRHEA. /ZINC & ZINC CMPD/ [Browning, E. Toxicity of Industrial Metals. 2nd ed. New York: Appleton-Century-Crofts, 1969. , p. 351] **PEER REVIEWED**

..UMAN TOXICITY EXCERPTS

ZINC SALTS ARE RELATIVELY NONTOXIC OWING TO EFFICIENT ZINC HOMEOSTATIC MECHANISM ... /ZINC SALTS/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 72] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

CHRONIC ZINC POISONING FROM DUST OR FUME IS QUESTIONABLE. ... /DATA/ INDICATE THAT RELATIVELY LARGE AMT OF ZINC MAY PASS FOR YEARS THROUGH KIDNEYS & GASTROINTESTINAL TRACT WITHOUT CAUSING ANY DETECTABLE CLINICAL DAMAGE. /ZINC CMPD/ [Browning, E. Toxicity of Industrial Metals. 2nd ed. New York: Appleton-Century-Crofts, 1969. , p. 353] **PEER REVIEWED**

UMAN TOXICITY EXCERPTS

... TAKEN BY MOUTH ARE RELATIVELY NON-TOXIC, THOUGH THE SOLUBLE SALTS IN LARGE DOSES MAY CAUSE VOMITING & DIARRHEA. /ZINC & ZINC CMPD/ [Browning, E. Toxicity of Industrial Metals. 2nd ed. New York: Appleton-Century-Crofts, 1969. , p. 351] **PEER REVIEWED**

..UMAN TOXICITY EXCERPTS

ZINC SALTS OF STRONG MINERAL ACIDS ARE ASTRINGENT, CORROSIVE TO SKIN, & IRRITATION TO GI TRACT; WHEN INGESTED THEY ACT AS EMETICS. ... THE EMITIC CONCN RANGE IN WATER IS FROM 675 TO 2280 PPM ... /ZINC SALTS/ [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2039] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

LARGE DOSES OF ZINC SALTS PRODUCE GENERAL SIGNS OF ACUTE METAL POISONING, IE VIOLENT VOMITING, PURGATION, EVIDENCE OF ABDOMINAL PAIN & COLLAPSE. CATTLE ... SHOW DRAMATIC DROP IN MILK YIELD. SOME ANIMALS BECOME SOMNOLENT & DEVELOP PARESIS. ... POST MORTEM LESIONS INCLUDE PULMONARY EMPHYSEMA, PALE, FLABBY MYOCARDIUM, PETECHIAE IN KIDNEYS, AND DEGENERATIVE CHANGES IN LIVER. /ZINC CMPD/ [Clarke, M. L., D. G. Harvey and D. J. Humphreys. Veterinary Toxicology. 2nd ed. London:

Bailliere Tindall, 1981. , p. 77] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

ATTEMPTS TO PRODUCE ZINC TOXICITY ... /WITH/ 0.25% IN DIET OF RATS HAVE NOT BEEN SUCCESSFUL. AT LEVELS ABOVE THIS HOMEOSTATIC MECHANISM BREAKS DOWN; GROWTH RETARDATION, HYPOCHROMIC ANEMIA & DEFECTIVE MINERALIZATIONS OF BONE OCCUR. DISPLACEMENT OF COPPER & ALTERED PHOSPHATASE ACTIVITY ARE PERHAPS MECHANISMS OF ACTION. /ZINC SALTS/ [Doull, J., C.D. Klaassen, and M. D. Amdur (eds.). Casarett and Doull's Toxicology. 2nd ed. New York: Macmillan Publishing Co., 1980. , p. 462] **PEER REVIEWED**

ON-HUMAN TOXICITY EXCERPTS

SYMPTOMS OF ZINC TOXICITY ARE LASSITUDE, SLOWER TENDON REFLEXES, BLOODY ENTERITIS, DIARRHEA, LOWERED LEUKOCYTE COUNT AND DEPRESSION OF CNS ... AND PARALYSIS OF EXTREMITIES. /ZINC CMPD/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 72] **PEER REVIEWED**

BSORPTION, DISTRIBUTION AND EXCRETION

... IDENTIFIED IN TISSUES OF CONJUNCTIVAE & LIDS OF TWO CHILDREN WHO WERE ACCIDENTLY SQUIRTED IN EYE WITH MATERIAL FROM THE LIQUID CENTER OF GOLF BALLS. [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. 991] **PEER REVIEWED**

ABSORPTION, DISTRIBUTION AND EXCRETION

The gastrointestinal absorption of soluble zinc salts in mammals is highly variable; it averages about 50% of the dietary intake and is dependent upon the zinc level in the diet. ... When small amounts of zinc are fed to experimental animals and ruminants, the absorption of zinc may increase to 80% ... . /Zinc cmpd/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 70] **PEER REVIEWED**

BSORPTION, DISTRIBUTION AND EXCRETION

ZINC CONCN IN GASTRIC CONTENT, BLOOD, LIVER, KIDNEY, & MUSCLES OF SUICIDAL VICTIM WERE 22.8, 2.4, 5.3, 5.3, & 5.7 MG/100 G, RESPECTIVELY, VERSUS CORRESPONDING NORMAL LEVELS OF 1.9, 1.5, 8.0, 4.0, & 5.0 MG/100 G. /ZINC/ [GIEBELMANN R ET AL; DEUT GESUNDHEITSW 29 (29): 1378-9 (1974)] **PEER REVIEWED**

CHANISM OF ACTION

... Freshly formed fumes are ... composed of ... particles in range of 0.05 to 0.5 um, & ... /have/ increased activity when they come into contact with the alveolar walls of lung. As fumes age they become less reactive because they tend to agglomerate or form aggregates & settle out of atmosphere ... thereby reducing concn of reactive particluates in lung. ... The size of particles is important factor in producing the illness. ... Finely divided particles of metals /are/ so small that they behave much like a gas & act on the alveolar surfaces, affecting the lung tissue & not upper respiratory tract. /Zinc/ [International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I&II. Geneva, Switzerland: International Labour Office, 1983. , p. 1339] **PEER REVIEWED**

INTERACTIONS

SIMULTANEOUS ADMIN OF CADMIUM ENHANCES SOME ... EFFECTS OF ZINC DEFICIENCY. ... DECR GROWTH RATE & CORNEAL KERATINIZATION /WERE

OBSERVED/ AMONG RATS FED WITH MARGINAL LEVEL OF ZINC, WHEN 3.4 MG/KG OF CADMIUM WAS ADDED TO DRINKING WATER. ... ZINC CONTENT OF TESTES ... /ALSO/ DECR. /ZINC CMPD/ [Friberg, L., Nordberg, G.F., Kessler, E. and Vouk, V.B. (eds). Handbook of the Toxicology of Metals. 2nd ed. Vols I, II.: Amsterdam: Elsevier Science Publishers B.V., 1986. , p. 668] **PEER REVIEWED**

NTERACTIONS

... ZINC HAS BEEN SHOWN TO PREVENT INHIBITORY EFFECTS OF LEAD ON RED CELL ENZYME ALANINE DEHYDRATASE, PRESUMABLY BY INDUCING MORE SYNTHESIS OF ENZYME FOR WHICH ZINC IS ESSENTIAL COMPONENT. CLOSELY RELATED TO THIS ... INTERACTION IS RISE IN RED CELL ZINC PROTOPORPHYRIN LEVELS IN LEAD WORKERS AT LOW BLOOD LEAD LEVELS. /ZINC CMPD/ [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2043] **PEER REVIEWED**

NTERACTIONS

OCCURRENCE OF HYPOCHROMIC, MICROCYTIC ANEMIA IN RATS FOLLOWING INGESTION OF EXCESSIVE ZINC & REVERSAL OF THIS ANEMIA BY IRON SUPPLEMENTATION DEMONSTRATE INTERACTION BETWEEN THESE TWO METALS. ... /IT/ AFFECTS IRON METAB BY INCR IRON TURNOVER, DECR LIFE SPAN OF ERYTHROCYTES & DECR HEPATIC ACCUM OF IRON AS FERRITIN. /ZINC ION/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 75] **PEER REVIEWED**

INTERACTIONS

SEVERE ANEMIA IN RATS PRODUCED BY ZINC TOXICITY IS OVERCOME OR PREVENTED BY ADDN OF COPPER OR LIVER EXTRACT TO THEIR DIET. MOST SYMPTOMS OF ZINC INTOXICATION CAN BE REVERSED BY SUPPLEMENTS OF SOL COPPER SALTS TO DIET; /IT IS/ POSTULATED THAT EXCESS DIETARY ZINC REDUCE INTESTINAL ABSORPTION OF COPPER. /ZINC CMPD/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 75] **PEER REVIEWED**

NTERACTIONS

USING CHICKEN EMBRYOS IT WAS POSSIBLE TO SHOW THAT ZN2+ AT DOSE OF 67.3 UG COULD TOTALLY INHIBIT DAMAGE CAUSED BY 0.0256 UG CD2+. /ZINC CMPD/ [RIBAS B ET AL; ZENTRALBL ARBEITSMED, ARBEITSSCHUTZ PROPHYL 27 (4): 81 (1977)] **PEER REVIEWED**

INTERACTIONS

CADMIUM IS CLOSELY RELATED TO ZINC IN ITS ELECTRONIC CONFIGURATION, & THE TWO IONS INTERACT PHYSIOLOGICALLY. CADMIUM TENDS TO INCREASE REQUIREMENT FOR ZINC OR ... ZINC DECREASES BIOAVAILABILITY OF CADMIUM. /ZINC ION/ [National Research Council. Drinking Water and Health. Volume 3. Washington, DC: National Academy Press, 1980. , p. 316] **PEER REVIEWED**

TNTERACTIONS

It has been shown in human beings that oral administration of histidine will cause decreases in serum zinc and an increase in urinary zinc excretion. /Zinc/ [Henkin RI et al; Arch Neurol 32: 745 (1975) as cited in USEPA; Ambient Water Quality Criteria Doc: Zinc p.C-13 (1980) EPA 400/5-80-079] **PEER REVIEWED**

TURAL OCCURRING SOURCES

OCCURS IN NATURE AS THE MINERALS WURTZITE & SPHALERITE. [The Merck Index. 10th ed. Rahway, New Jersey: Merck Co., Inc.,

1983. , p. 1458] **PEER REVIEWED**

NATURAL OCCURRING SOURCES

... ABOVE A RATIO OF FE:ZN OF 1:5 THE MINERAL IS CALLED MARMATITE; ABOVE 5:6 SPHALERITE STRUCTURE CEASES TO EXIST. NEXT TO FE, CD IS MOST COMMON IMPURITY IN SPHALERITE ... GALLIUM & GE ALSO OCCUR IN SPHALERITE (LOW TEMP FORMATION); SN & INDIUM OCCUR IN TRACES FROM HIGH TEMP DEPOSITS. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2033] **PEER REVIEWED**

ROBABLE ROUTES OF HUMAN EXPOSURE

Zinc poisoning is mostly accidential from the intake of pesticides, inadevertant therapeutic use of heavy doses of zinc salts, or drinking of acidic juices or brews made in galvanized iron utensils. /Zinc compounds/ [Venugopal, B. and T.D. Luckey. Metal Toxicity in Mammals, 2. New York: Plenum Press, 1978. , p. 69] **PEER REVIEWED**

ATER STANDARDS

Toxic pollutant designated pursuant to section 307(a)(1) of the Clean Water Act and is subject to effluent limitations. /Zinc and compounds/ [40 CFR 401.15 (7/1/87)] **PEER REVIEWED**

ATER STANDARDS

The secondary contaminant level of zinc for public water systems is 5 mg/l. These regulations control contaminants in drinking water that primarily affect the aesthetic qualities relating to the public acceptance of drinking water. The States may establish higher or lower levels which may be appropriate dependent, upon local conditions such as unavailability of alternate source waters or other compelling factors, provided that public health and welfare are not adversely affected. /Soluble zinc salts/ [40 CFR 143 (7/1/87)] **PEER REVIEWED**

ATER STANDARDS

For total recoverable zinc the criterion to protect freshwater aquatic life ... is 47 ng/l as a 24 hr average ... at hardnesses of 50, 100, and 200 mg/l as CaCO3 otal recoverable zinc should not exceed 180, 320, 570 ug/l y time. /Soluble zinc salts/ [USEPA/OWRS; Quality Criteria for Water 1986 Zinc (1986) EPA 440/5-86-001] **PEER REVIEWED**

ATER STANDARDS

For total recoverable zinc the criterion to protect saltwater aquatic life ... is 58 ug/l as a 24 hr average and the concentration should not exceed 170 ug/l at any time. /Soluble zinc salts/ [USEPA/OWRS; Quality Criteria for Water 1986 Zinc (1986) EPA 440/5-86-001] **PEER REVIEWED**

A REQUIREMENTS

Zinc Sulfide is an indirect food additive for use only as a component of adhesives. [21 CFR 175.105 (4/1/88)] **PEER REVIEWED**

A REQUIREMENTS

Bottled water shall, when a composite of analytical units of equal volume from a sample is examined by the methods described in paragraph (d)(1)(ii) of this section, meet the standards of chemical quality and shall not contain zinc in excess of 5.0 mg/l. /Soluble zinc salts/ [21 CFR 103.35 (4/1/86)] **PEER REVIEWED**

FDA REQUIREMENTS

Rubber articles intended for repeated use may be safely used in

producing, manufacturing, packing, processing, preparing, treating, packaging, trasporting, or holding food, subject to the provisions of this section. Zinc sulfide is used in fillers. [21 CFR 177.2600 (4V) (4/1/88)] **PEER REVIEWED**

RCRA REQUIREMENTS

A solid waste containing zinc sulfide may become characterized as a hazardous waste when subjected to the Toxicant Extraction Procedure listed in 40 CFR 261.24, and if so characterized, must be managed as a hazardous waste. [40 CFR 261.24 (7/1/87)] **PEER REVIEWED**

AMPLING PROCEDURES

Analyte: zinc; Matrix: air; Sampler: filter (0.8-um cellulose ester membrane); Flow rate: 1-3 l/min; Vol: min: 2 l at 5 mg/cu m, max: 400 l; Stability: stable /Zinc & cmpd, as zinc/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 7030-1] **PEER REVIEWED**

AMPLING PROCEDURES

Analyte: Zinc; Specimen: Blood or tissue; Vol: 10 ml blood, or 1 g tissue; Preservative: Heparin for blood, none for tissue; Controls: collect 3 blood specimens from unexposed workers; Stability: not established /Elements in blood or tissue/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V1 8005-1] **PEER REVIEWED**

SAMPLING PROCEDURES

Analyte: Zinc; Matrix: urine; Vol: 50-200 ml in polyethylene bottle; Preservative: 5 ml concn nitric acid added after collection; Controls: collect at least 3 urine specimens from unexposed workers; Stability: not established /Total metals in urine/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V1 8310-1] **PEER REVIEWED**

AMPLING PROCEDURES

Sample volumes required depend upon the number of different digestion procedures necessary for analysis. Samples are collected in either polyethylene or glass containers. Preservation of the sample is maintained by adjusting the pH<2 with nitric acid. Maximum holding time is 6 months. ... Solid samples must be at least 200 g and usually require no preservation other that storing at 4 deg C until analyzed. /Total metals (except hexavalent chromium and mercury)/ [USEPA; Test Methods for Evaluating Solid Waste. Physical/Chemical Methods 3rd Ed (1986) EPA 955-001-00000-1] **PEER REVIEWED**

NALYTIC LABORATORY METHODS

Analyte: Zinc; Matrix: air; Procedure: Flame atomic absorption; Wave length: 213.9 nm; Range: 10-100 ug/sample; Est LOD: 3 ug/samp; Precision: 0.03; Interferences: none known /Zinc and cmpd, as Zn/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 7030-1] **PEER REVIEWED**

ALYTIC LABORATORY METHODS

WATER SAMPLES ANALYZED BY ATOMIC ABSORPTION: BROOKS RR, PRESLEY BJ & IR KAPLAN; TALANTA 14: 809 (1967); TENNY AM; INSTRUMENT

NEWS 18: 14 (1967); FISHMAN MJ; ATOMIC ABSORPTION NEWSLETTER 5: 102 (1966). /TOTAL ZINC/ [Sunshine, I. (ed.). CRC Handbook of Analytical Toxicology. Cleveland: The Chemical Rubber Co., 1969. , p. 975] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
FERNANDEZ & MANNING (1971) & SURLES ET AL (1975) ... DEMONSTRATED USE OF GRAPHITE FURNACE TO INCR SAMPLE ATOMIZATION FOR FRESH-WATER ANALYSIS, WITH ZINC DETECTION LIMIT OF 0.001 UG/L. /TOTAL ZINC/ [National Research Council. Drinking Water & Health Volume 1. Washington, DC: National Academy Press, 1977. , p. 301] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
EMISSION SPECTROGRAPHIC METHOD: DIRECT CURRENT ARC EXCITATION, ALTERNATING CURRENT SPARK EXCITATION. /TOTAL ZINC/ [Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through 11/867 44.003] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
SURFACE & SALINE WATERS, & DOMESTIC & INDUSTRIAL WASTES: ATOMIC ABSORPTION SPECTROPHOTOMETER METHODS. /TOTAL ZINC/ [Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through 12/557 33.089] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
RESIDUES IN FOOD, 33.089. ATOMIC ABSORPTION SPECTROPHOTOMETER METHODS. 49.001. PLANT ANALYSIS. METHOD MAY BE ADAPTED TO OTHER AGRICULTURAL & BIOLOGICAL MATERIALS; EMISSION SPECTROGRAPHIC METHODS. /TOTAL ZINC/ [Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through 12/1094 2.096] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
Analyte: Zinc; Matrix: air; Procedure: atomic absorption spectrophotometry; Range: 0.1 to 1.0 ug/ml, 4.2-42 ug/cu m with solution detection limit of 0.001 ug/ml. /Total zinc/ [U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual of V5 173-1] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
EPA Method 7950. Direct Aspiration Atomic Absorption Spectroscopy for Zinc. This method is ... applicable to ... drinking, surface, and saline waters and domestic and industrial wastes. ... Ground water, other aqueous samples, EP extracts, industrial wastes, soil, sludges, sediments, and other solid wastes require digestion prior to analysis. ... The optimum concentration range is 0.05-1 mg/l with a wavelength of 213.9 nm, sensitivity is 0.02 mg/l, and a detection limit of 0.005 mg/l. /Total zinc/ [USEPA; Test Methods for Evaluating Solid Waste. Physical/Chemical Methods 3rd Ed (1986) EPA 955-001-00000-1] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
MINOR NUTRIENTS IN FERTILIZERS, 25.143. RESIDUES IN FOOD, & 33.089. ATOMIC ABSORPTION SPECTROPHOTOMETER METHODS. 49.001.

PLANT ANALYSIS. METHOD MAY BE ADAPTED TO OTHER AGRICULTURAL & BIOLOGICAL MATERIALS; EMISSION SPECTROGRAPHIC METHODS. /TOTAL ZINC/ [Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through 12/1094 2.096] **PEER REVIEWED**

NALYTIC LABORATORY METHODS

ZINC IN FERTILIZERS: ATOMIC ABSORPTION METHOD FOR ZINC AS MINOR NUTRIENT; 2.151. GRAVIMETRIC METHOD FOR SAMPLES CONTAINING EQUAL TO OR GREATER THAN 0.1%; 2.152. COLORIMETRIC METHOD USING DITHIZONE FOR SAMPLES CONTAINING LESS THAN 4%; 2.153-2.159. ZINCON ION EXCHANGE METHOD. /TOTAL ZINC/ [Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through 13/20 2.109] **PEER REVIEWED**

NALYTIC LABORATORY METHODS

Analyze samples within 6 hr after collection. Addition of hydrochloric acid (HCl) preserves the metallic ion content but requires that: (a) the acid be zinc free; (b) the sample bottles be rinsed with acid before use; and (c) the samples be evaporated to dryness in silica dishes to remove excess hydrochloric acid (HCl) before analysis. ... The reaction of zinc with dithizone produces colored coordination compounds that are extractable into organic solvents such as carbon tetrachloride. Most interferences can be overcome by adjusting the pH to 4.0 to 5.5 and by adding sufficient sodium thiosulfate. Minimum detectable quantity is 1 ug Zn. /Total zinc/ [Franson MA (Ed); Standard Methods for the Examination of Water and Wastewater p. 255-57 (1985)] **PEER REVIEWED**

NALYTIC LABORATORY METHODS

Analyze samples within 6 hr after collection. Addition of hydrochloric acid (HCl) preserves the metallic ion content but requires that: (a) the acid be zinc free; (b) the sample bottles be rinsed with acid before use; and (c) the samples be evaporated to dryness in silica dishes to remove excess hydrochloric acid (HCl) before analysis. ... Zinc is separated from other metals by extraction with dithizone and is determined by measuring the color of the zinc-dithizone complex in carbon tetrachloride (CCl4). Specificity in the separation is achieved by extracting from a nearly neutral solution containing bis(2-hydroxyethyl)dithiocarbamyl ion and cyanide ion. This method is intended for the examination of polluted water supplies. /Total zinc/ [Franson MA (Ed); Standard Methods for the Examination of Water and Wastewater p.257-59 (1985)] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

Analyze samples within 6 hr after collection. Addition of hydrochloric acid (HCl) preserves the metallic ion content but requires that: (a) the acid be zinc free; (b) the sample bottles be rinsed with acid before use; and (c) the sample bottles be evaporated to dryness in silica dishes to remove excess hydrochloric acid (HCl) before analysis. ... In this colorimetric method, zinc forms a blue complex with 2-carboxy-2'-hydroxy-5'-sulfoformazyl benzene (zincon) in a

solution buffered to pH 9.0. Cyanide is added to complex zinc and heavy metals. Cyclohexanone is added to free zinc selectively from its cyanide complex so that it can be complexed with zincon to form a blue color. Sodium ascorbate reduces manganese interference. The developed color is stable except in the presence of copper. Minimum detectable concentration is 0.02 mg Zn/l. This method can be used for the examination of polluted or unpolluted water supplies. /Total zinc/ [Franson MA (Ed); Standard Methods for the Examination of Water and Wastewater p.259-61 (1985)] **PEER REVIEWED**

LINICAL LABORATORY METHODS

Analyte: Zinc; Matrix: blood or tissue; Procedure: Inductively-coupled argon plasma-atomic emission spectroscopy; Wavelength: 213.9 nm; Range: 10 to 10,000 ug/100 g blood, 2 to 2000 ug/g tissue; Est LOD: 1 ug/100 g blood, 0.2 ug/g tissue; Precision: 17 (% Sr); Interferences: spectral, minimized by wavelength selection. /Elements in blood or tissue/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V1 8005-1] **PEER REVIEWED**

LINICAL LABORATORY METHODS

Analyte: Zinc; Matrix: urine; Procedure: Inductively-coupled argon-plasma, atomic emmission spectroscopy; Extraction media: polydithiocarbamate resin; Wavelength: 213.9; Range: 0.25-200 ug/samp; Est LOD: 0.1 ug/samp; Precision: 0.089; Interferences: spectral, minimized by wavelength selection /Metals in urine/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V1 8310-1] **PEER REVIEWED**

CLINICAL LABORATORY METHODS

URINE, SERUM & WHOLE BLOOD; AA SPECTROPHOTOMETRY. HACKLEY BM ET AL, A SIMPLIFIED METHOD FOR PLASMA ZINC DETERMINATION BY ATOMIC-ABSORPTION SPECTROPHOTOMETRY, CLIN CHEM, 14, 1, 1968. DAWSON JB ET AL, DIRECT DETERMINATION OF ZINC IN WHOLE BLOOD, PLASMA & URINE BY AA SPECTROSCOPY, CLIN CHIM ACTA, 26, 465, 1969. /TOTAL ZINC/ [Sunshine, Irving (ed.) Methodology for Analytical Toxicology. Cleveland: CRC Press, Inc., 1975., p. 384] **PEER REVIEWED**

LINICAL LABORATORY METHODS

DAWSON JB & WALKER BG, DIRECT DETERMINATION OF ZINC IN WHOLE BLOOD, PLASMA & URINE BY ATOMIC ABSORPTION SPECTROSCOPY, CLIN CHIM ACTA, 26, 465, 1969. CARTER P, SPECTROPHOTOMETRIC SUBMICROGRAM SERUM ZINC ASSAY APPLICATION FOR ROUTINE SERVICE LAB, CLIN CHIM ACTA, 52, 277, 1974. /TOTAL ZINC/ [Sunshine, Irving (ed.) Methodology for Analytical Toxicology. Cleveland: CRC Press, Inc., 1975. , p. 387] **PEER REVIEWED**

LINICAL LABORATORY METHODS

ZINC MAY BE DETERMINED BY ATOMIC ABSORPTION SPECTROPHOTOMETRY BY ASPIRATION OF DILUTED SAMPLES OF BIOLOGICAL FLUIDS /URINE, BLOOD, & SERUM/: MALSTROM, G, DETERMINATION OF ZINC IN BIOLOGICAL MATERIALS, IN METHODS OF BIOCHEM ANALYSIS, VOL 3, GLICK, D, ED, INTERSCIENCE, NY, 1956, P 327. /TOTAL ZINC/ [Sunshine, Irving (ed.) Methodology for Analytical Toxicology. Cleveland: CRC Press, Inc., 1975. , p. 384] **PEER REVIEWED**

SPECIAL REPORTS

USEPA; Ambient Water Quality Criteria Doc: Zinc (1980) EPA 400/5-80-079

PECIAL REPORTS

USEPA; Ambient Water Quality Criteria Doc: Zinc (1987) EPA 440/5-87-003

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um PVC membrane); flow rate: 1.7 l/min; vol: min: 75 l at 5 mg/cu m, max: 1000 l at 5 mg/cu m; Stability: indefinite /Nuisance dust, respirable/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 600-1] **PEER REVIEWED**

AMPLING PROCEDURES

Analyte: Air borne particulate material; Matrix: Air; Sampler: filter (tared 37-mm, 5-um PVC filter); Flow rate: 1.5-2 l/min; Vol: min: 25 l at 15 mg/cu m, max: 133 l at 15 mg/cu m; Stability: indefinite /Nuisance dust, total/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 500-1] **PEER REVIEWED**

AMPLING PROCEDURES

Analyte: Zinc (metals and oxides); Matrix: air; Sampler: filter (0.8 um cellulose ester membrane); Flow rate: 1 l/min; Vol: min: 10 l, max: 400 l; Stability: At least 1 yr at 25 deg C /Welding and brazing fumes/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 7200-1] **PEER REVIEWED**

SAMPLING PROCEDURES

Sample volumes required depend upon the number of different digestion procedures necessary for analysis. Samples are collected in either polyethylene or glass containers. Preservation of the sample is maintained by adjusting the pH< 2 with nitric acid. Maximum holding time is 6 months. ... Solid samples must be at least 200 g and usually require no preservation other that storing at 4 deg C until analyzed. /Total metals (except hexavalent chromium and mercury)/ [USEPA; Test Methods for Evaluating Solid Waste. Physical/Chemical Methods 3rd Ed (1986) EPA 955-001-00000-1] **PEER REVIEWED**

AMPLING PROCEDURES

Samples of zinc oxide are collected ... using a sampler with a Cellulose Ester Memebrane Filter. The filter is a 0.8 um pore size mixed Cellulose Ester Memebrane mounted in a closed-face sampling cassette which can be attached to the worker near his breathing zone. /Zinc oxide in air/ [NIOSH; Criteria Document: Zinc Oxide p.59 (1975) DHEW Pub. NIOSH 76-104] **PEER REVIEWED**

ALYTIC LABORATORY METHODS

PARTICULATE MATTER IS COLLECTED FROM AIR ON MEMBRANE FILTER & ANALYZED DIRECTLY FOR CRYSTALLINE ZINC OXIDE BY X-RAY DIFFRACTION. RANGE OF METHOD IS FROM 5-500 UG OF ZINC OXIDE/SQ CM OF FILTER SURFACE. THIS CORRESPONDS TO 25-2000 UG OF ZINC OXIDE ON 25 MM FILTER, OR 1-80 MG/CU M IN 25 L OF AIR. [U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual of V1 222-1] **PEER REVIEWED**

ALYTIC LABORATORY METHODS

ZINC OXIDE FUME IS ANALYZED IN AIR SAMPLES BY X-RAY DIFFRACTION AFTER COLLECTION ON FILTER. THIS METHOD WAS VALIDATED ... OVER RANGE OF 2.4-9.9 MG/CU M FOR A 180 L SAMPLE AT ATMOSPHERIC TEMP & PRESSURE IN RANGE OF 20-22 DEG C & 760-767 MM HG. [U.S.

Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual of V3 S316-1] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
Analyte: Zinc; Matrix: air; Procedure: Flame atomic absorption; Wave length: 213.9 nm; Range: 10-100 ug/sample; Est LOD: 3 ug/samp; Precision: 0.03; Interferences: none known /Zinc and cmpd, as Zn/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 7030-1] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
Analyte: Zinc oxide, crystalline, direct analysis on filter; Matrix: air; Procedure: X-ray powder diffraction; Range: 50-2000 ug/samp; Est LOD: 5 ug/ samp; Precision: 0.15 @ 1 mg/cu m, 0.05 for greater than 2 mg/cu m; Interferences: Fe2O3, Zn, Zn(NH3)2Cl2, (NH4)3ZnCl5, (NH4)2ZnCl4, (NH4)2Zn(SO4)2.6H2O resolved by using alternate peaks. [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 7502-1] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
Analyte: Mass of respirable dust fraction; Matrix: air; Procedure: Gravimetric (filter weighing); Range: 0.3-2 mg/sample; Est LOD: 0.2 mg/samp; Precision: 68 ug with 0.01 mg sensitivity balance; Interferences: larger than respirable particles (10 um) /Nuisance dust, respirable/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 600-1] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
Analyte: Air borne particulate material; Matrix: Air; Procedure: Gravimetric (filter weight); Range: 0.3-2 mg/sample; Est LOD: 0.2 mg/samp; Precision: 0.08 mg/sample; Interferences: organic and particulate matter may be removed by dry ashing /Nuisance dust, total/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 500-1] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
WATER SAMPLES ANALYZED BY ATOMIC ABSORPTION: BROOKS RR, PRESLEY BJ & IR KAPLAN; TALANTA 14: 809 (1967); TENNY AM; INSTRUMENT NEWS 18: 14 (1967); FISHMAN MJ; ATOMIC ABSORPTION NEWSLETTER 5: 102 (1966). /TOTAL ZINC/ [Sunshine, I. (ed.). CRC Handbook of Analytical Toxicology. Cleveland: The Chemical Rubber Co., 1969. , p. 975] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
FERNANDEZ & MANNING (1971) & SURLES ET AL (1975) ... DEMONSTRATED USE OF GRAPHITE FURNACE TO INCR SAMPLE ATOMIZATION FOR FRESH-WATER ANALYSIS, WITH ZINC DETECTION LIMIT OF 0.001 UG/L. /TOTAL ZINC/ [National Research Council. Drinking Water & Health Volume 1. Washington, DC: National Academy Press, 1977. , p. 301] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS
EMISSION SPECTROGRAPHIC METHOD: DIRECT CURRENT ARC EXCITATION,

ALTERNATING CURRENT SPARK EXCITATION. /TOTAL ZINC/ [Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through 11/867 44.003] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

SURFACE & SALINE WATERS, & DOMESTIC & INDUSTRIAL WASTES: ATOMIC ABSORPTION SPECTROPHOTOMETER METHODS. /TOTAL ZINC/ [Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through 12/557 33.089] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

ZINC IN FERTILIZERS: ATOMIC ABSORPTION METHOD FOR ZINC AS MINOR NUTRIENT; 2.151. GRAVIMETRIC METHOD FOR SAMPLES CONTAINING EQUAL TO OR GREATER THAN 0.1%; 2.152. COLORIMETRIC METHOD USING DITHIZONE FOR SAMPLES CONTAINING LESS THAN 4%; 2.153-2.159. ZINCON ION EXCHANGE METHOD. /ZINC/ [Association of Official Analytical Chemists. Official Methods of Analysis. 10th ed. and supplements. Washington, DC: Association of Official Analytical Chemists, 1965. New editions through 13/20 2.109] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

Analyte: Zinc; Matrix: air; Procedure: atomic absorption spectrophotometry; Range: 0.1 to 1.0 ug/ml, 4.2-42 ug/cu m with solution detection limit of 0.001 ug/ml. /Total zinc/ [U.S. Department of Health, Education Welfare, Public Health Service. Center for Disease Control, National Institute for Occupational Safety Health. NIOSH Manual of V5 173-1] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

Analyte: Zinc; Matrix: air; Procedure: X-ray fluorescence; Range: 0.05-0.06 mg/cu m; Est LOD: 2 ug each metal/samp Precision: 0.043; Interferences: Controlled with wavelength depressive fluorescence, more severe with energy depressive systems, cobalt in fumes requires different ratio standard element /Welding and brazing fumes/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V2 7200-1] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

ZINC, ZINC OXIDE, LEAD, THE 4 KNOWN ZINC CHROMATES, & RHOMBIC & MONOCLINIC LEAD CHROMATE WERE IDENTIFIED IN 0.3-0.5 MG PAINT SAMPLES BY X-RAY DIFFRACTOMETRY. THE ZINC CHROMATES WERE IDENTIFIABLE AT 7.0-9.3 ANGSTROMS. THE METHOD COULD BE USED TO IDENTIFY, BUT NOT TO QUANTITATE ZINC CHROMATES ON FILTERS OF AIR SAMPLES FROM AREAS USED FOR SPRAY PAINTING. [ALTIERI A ET AL; ANN IST SUPER SANITA 13 (1-2): 315-9 (1977)] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

EPA Method 7950: Direct Aspiration Atomic Absorption Spectroscopy for Zinc. This method is ... applicable to ... drinking, surface, and saline waters and domestic and industrial wastes. ... Ground water, other aqueous samples, EP extracts, industrial wastes, soil, sludges, sediments, and other solid wastes require digestion prior to analysis. ... The

optimum concentration range is 0.05-1 mg/l with a wavelength of 213.9 nm, sensitivity is 0.02 mg/l, and a detection limit of 0.005 mg/l. /Total zinc/ [USEPA; Test Methods for Evaluating Solid Waste. Physical/Chemical Methods 3rd Ed (1986) EPA 955-001-00000-1] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

The sample ... is ashed using nitric acid to destroy the organic matrix. The zinc is solubilized in an acidic solution maintaining a pH of 1. Samples, Blanks, and Standards are aspirated into the Atomic Absorbtion Flame. A hollow cathode lamp for zinc provides the characteristic line. The absorption of this line by the Ground State Atoms in the flame is proportional to the Zn in the aspirated sample. The optimum working range is 0.025-2 ug Zn/ml. This value can be extended to higher concentrations by dilution of the sample. The sensitivity is 0.025 ug Zn/ml. This value will vary somewhat depending on the instrument used. /Zinc oxide in air/ [NIOSH; Criteria Document: Zinc Oxide p.63 (1975) DHEW Pub. NIOSH 76-104] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

Analyze samples within 6 hr after collection. Addition of hydrochloric acid (HCl) preserves the metallic ion content but requires that: (a) the acid be zinc free; (b) the sample bottles be rinsed with acid before use; and (c) the samples be evaporated to dryness in silica dishes to remove excess hydrochloric acid (HCl) before analysis. ... The reaction of zinc with dithizone produces colored coordination compounds that are extractable into organic solvents such as carbon tetrachloride. Most interferences can be overcome by adjusting the pH to 4.0 to 5.5 and by adding sufficient sodium thiosulfate. Minimum detectable quantity is 1 ug Zn. /Total zinc/ [Franson MA (Ed); Standard Methods for the Examination of Water and Wastewater p. 255-57 (1985)] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

Analyze samples within 6 hr after collection. Addition of hydrchloric acid (HCl) preserves the metallic ion content but requires that: (a) the acid be zinc free; (b) the sample bottles be rinsed with acid before use; and (c) the samples be evaporated to dryness in silica dishes to remove excess hydrochloric acid (HCl) before analysis. ... Zinc is separated from other metals by extraction with dithizone and is determined by measuring the color of the zinc-dithizone complex in carbon tetrachloride (CCl4). Specificity in the separation is achieved by extracting from a nearly neutral solution containing bis(2-hydroxyethyl)dithiocarbamyl ion and cyanide ion. This method is intended for the examination of polluted water supplies. /Total zinc/ [Franson MA (Ed); Standard Methods for the Examination of Water and Wastewater p.257-59 (1985)] **PEER REVIEWED**

ANALYTIC LABORATORY METHODS

Analyze samples within 6 hr after collection. Addition of hydrochloric acid (HCl) preserves the metallic ion content but requires that: (a) the acid be zinc free; (b) the sample bottles be rinsed with acid before use; and (c) the sample bottles be evaporated to dryness in silica dishes to remove

excess hydrochloric acid (HCl) before analysis. ... In this colorimetric method, zinc forms a blue complex with 2-carboxy-2'-hydroxy-5'-sulfoformazyl benzene (zincon) in a solution buffered to pH 9.0. Cyanide is added to complex zinc and heavy metals. Cyclohexanone is added to free zinc selectively from its cyanide complex so that it can be complexed with zincon to form a blue color. Sodium ascorbate reduces manganese interference. The developed color is stable except in the presence of copper. Minimum detectable concentration is 0.02 mg Zn/l. This method can be used for the examination of polluted or unpolluted water supplies. /Total zinc/ [Franson MA (Ed); Standard Methods for the Examination of Water and Wastewater p.259-61 (1985)] **PEER REVIEWED**

LINICAL LABORATORY METHODS

Analyte: Zinc; Matrix: blood or tissue; Procedure: Inductively-coupled argon plasma-atomic emission spectroscopy; Wavelength: 213.9 nm; Range: 10 to 10,000 ug/100 g blood, 2 to 2000 ug/g tissue; Est LOD: 1 ug/100 g blood, 0.2 ug/g tissue; Precision: 17 (% Sr); Interferences: spectral, minimized by wavelength selection /Elements in blood or tissue/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V1 8005-1] **PEER REVIEWED**

LINICAL LABORATORY METHODS

Analyte: Zinc; Matrix: urine; Procedure: Inductively-coupled argon-plasma, atomic emmission spectroscopy; Extraction media: polydithiocarbamate resin; Wavelength: 213.9; Range: 0.25-200 ug/samp; Est LOD: 0.1 ug/samp; Precision: 0.089; Interferences: spectral, minimized by wavelength selection /Metals in urine/ [U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH V1 8310-1] **PEER REVIEWED**

LINICAL LABORATORY METHODS

URINE, SERUM & WHOLE BLOOD; AA SPECTROPHOTOMETRY. HACKLEY BM ET AL, A SIMPLIFIED METHOD FOR PLASMA ZINC DETERMINATION BY ATOMIC-ABSORPTION SPECTROPHOTOMETRY, CLIN CHEM, 14, 1, 1968. DAWSON JB ET AL, DIRECT DETERMINATION OF ZN IN WHOLE BLOOD, PLASMA & URINE BY AA SPECTROSCOPY, CLIN CHIM ACTA, 26, 465, 1969. /TOTAL ZINC/ [Sunshine, Irving (ed.) Methodology for Analytical Toxicology. Cleveland: CRC Press, Inc., 1975. , p. 384] **PEER REVIEWED**

LINICAL LABORATORY METHODS

DAWSON JB & WALKER BG, DIRECT DETERMINATION OF ZINC IN WHOLE BLOOD, PLASMA & URINE BY ATOMIC ABSORPTION SPECTROSCOPY, CLIN CHIM ACTA, 26, 465, 1969. CARTER P, SPECTROPHOTOMETRIC SUBMICROGRAM SERUM ZINC ASSAY APPLICATION FOR ROUTINE SERVICE LAB, CLIN CHIM ACTA, 52, 277, 1974. /TOTAL ZINC/ [Sunshine, Irving (ed.) Methodology for Analytical Toxicology. Cleveland: CRC Press, Inc., 1975. , p. 387] **PEER REVIEWED**

LINICAL LABORATORY METHODS

ZINC MAY BE DETERMINED BY ATOMIC ABSORPTION SPECTROPHOTOMETRY BY ASPIRATION OF DILUTED SAMPLES OF BIOLOGICAL FLUIDS /URINE, BLOOD, & SERUM/: MALSTROM, G, DETERMINATION OF ZINC IN

BIOLOGICAL MATERIALS, IN METHODS OF BIOCHEM ANALYSIS, VOL 3, GLICK, D, ED, INTERSCIENCE, NY, 1956, P 327. /TOTAL ZINC/
[Sunshine, Irving (ed.) Methodology for Analytical Toxicology. Cleveland: CRC Press, Inc., 1975. , p. 384] **PEER REVIEWED**

SPECIAL REPORTS
USEPA; Ambient Water Quality Criteria Doc: Zinc (1980) EPA 400/5-80-003]

SPECIAL REPORTS
USEPA; Ambient Water Quality Criteria Doc: Zinc (1987) EPA 440/5-87-003

March 12, 1991
Project No: 400754

APPENDIX G

Zinc Sulfide

Du Pont Environmental Remediation Services

PROG:
SR (ZNS (MF))
ONE- :

SS 2 /C?
USER:

PROG:
NP ()

SS 2 /C?
USER:
PRT DL -36
PROG:

CHEMLINE

Zinc Sulfide

36
RN - 1314-98-3
ON - 37187-67-0 (CAS)
MF - S-Zn
N1 - Zinc sulfide [ZnS] (9CI)
SY - Albalith [HSDB]
SY - C.I. Pigment White 7 [CAS]
SY - HSDB 5802 [NLM]
SY - Irtran 2 [CAS:HSDB]
SY - Sachtolith [CAS:HSDB]
SY - ZINC MONOSULFIDE [HSDB]
SY - Zinc sulfide (8CI) [CAS:HSDB*:MESH]
LO - TOXLINE
LO - TOXLIT
LO - TOXLINE65
LO - TOXLIT65
LO - MED86
LO - MED83
LO - MED80
LO - MESH
LO - HSDB
LO - EINECS
LO - TSCAINV
EM - 9005

NATIONAL LIBRARY OF MEDICINE
CHEMLINE LOCATOR FILE

N - 1047-16-1
ON - 67053-84-3 (CAS)
MF - C20-H12-N2-O2
1 - Quino(2,3-b)acridine-7,14-dione, 5,12-dihydro- (8CI)(9CI)
SY - C.I. Pigment Violet 19 [CAS]
SY - CI 46500 [CTFA:HSDB]
Y - Cinquasia B-RT 796D [CAS]
Y - Cinquasia Red [CAS:HSDB*]
SY - Cinquasia Red B [CAS:HSDB]
SY - Cinquasia Red Y [CAS:HSDB]
Y - Cinquasia Red Y-RT 759D [CAS]
SY - Cinquasia Violet R [CAS:HSDB]
SY - Fastogen Super Red BN [CAS]
Y - Fastogen Super Red YE [CAS]
Y - Hostaperm Red E 3B [CAS:HSDB]
SY - HOSTAPERM RED E 5B [HSDB]
SY - Hostaperm Red Violet ER [CAS:HSDB]
SY - HSDB 6136 [NLM]
SY - MONASTRAL RED [HSDB]
SY - Monastral Red B [CAS:HSDB]
SY - Monastral Red Y [CAS:HSDB]
SY - Monastral Violet R [CAS:HSDB]
SY - Monolite Violet 4R [CAS]
SY - NSC 316165 [NLM]
SY - PALIOGEN RED BG [HSDB]
SY - Permanent Red E 3B [CAS]
SY - PERMANENT RED E3B [HSDB]
SY - PERMANENT RED E5B [HSDB]
SY - Pigment Pink Quinacridone S [CAS]
SY - PIGMENT QUINACRIDONE RED [HSDB]
SY - Pigment Violet 19 [CTFA*]
SY - PV Fast Red E 3B [CAS:HSDB]
SY - PV Fast Red E 5B [CAS:HSDB]
SY - Quinacridone [CAS:HSDB]
SY - QUINACRIDONE RED MC [HSDB]
SY - Quinacridone violet [CAS:HSDB]
SY - QUINACRIDONE VIOLET MC [HSDB]
SY - Quino(2,3-b)Acridine-7,14-dione, 5,12-Dihydro- [CTFA:HSDB]
SY - 5,12-Dihydroquino(2,3-b)Acridine-7,14-dione [CTFA:HSDB]
NR - 5
RS - 6,6,6,6,6
RE - C5N-C5N-C6-C6-C6
LO - TOXLIT
LO - TOXLINE65
LO - HSDB
LO - EINECS
LO - TSCAINV
EM - 9005

NATIONAL LIBRARY OF MEDICINE/TOXNET

HAZARDOUS SUBSTANCES DATABANK [HSDB]
(Some data in this file may not be peer reviewed.)

ZINC SULFIDE CAS RN = 1314-98-3

1 - HSDB	
AZARDOUS SUBSTANCES DATABANK NUMBER	5802
LAST REVISION DATE	901023
REVIEW DATE	Reviewed by SRP on 5/20/88
PDATE HISTORY	Field update on 11/09/90, 1 field added/edited/deleted.
UPDATE HISTORY	Complete Update on 10/23/90, 1 field added/edited/deleted.
PDATE HISTORY	Field update on 12/29/89, 1 field added/edited/deleted.
PDATE HISTORY	Complete Update on 04/05/89, 49 fields added/edited/deleted.
PDATE HISTORY	Complete Update on 06/04/85
RECORD LENGTH	42200
AME OF SUBSTANCE	**ZINC SULFIDE**
AS REGISTRY NUMBER	**1314-98-3**
SYNONYMS	ZINC SULFIDE (ZNS) **PEER REVIEWED**
YNONYMS	ALBALITH **PEER REVIEWED**
ONYMS	IRTRAN 2 **PEER REVIEWED**
ONYMS	ZINC MONOSULFIDE **PEER REVIEWED**
SYNONYMS	CI Pigment White 7 **PEER REVIEWED**
YNONYMS	Sachtolith **PEER REVIEWED**
YNONYMS	Zinc blende **PEER REVIEWED**
MOLECULAR FORMULA	S-Zn **PEER REVIEWED**
PA HAZARDOUS WASTE NUMBER	D003; A waste containing zinc sulfide may (or may not) be characterized a hazardous waste following testing by the Toxicant Extraction Procedure as prescribed by the Resource Conservation and Recovery Act (RCRA) regulations.
RELATED HSDB RECORDS	1063 [ZINC SULFATE]
ELATED HSDB RECORDS	1344 [ZINC]

ETHODS OF MANUFACTURING

REACTION OF ZINC SULFATE WITH SODIUM SULFIDE FOLLOWED BY CALCINATION; PASSAGE OF HYDROGEN SULFIDE INTO AN AQUEOUS SOLUTION OF A ZINC SALT [SRI] **PEER REVIEWED**

FORMULATIONS/PREPARATIONS

GRADES: TECHNICAL; CP, FLUORESCENT OR LUMINOUS; SINGLE CRYSTALS. [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987. , p. 1257] **PEER REVIEWED**

ORMULATIONS/PREPARATIONS

3-12 mm and -325 mesh, 99.9 and 99.99% purity grades [Kuney, J.H. and J.N. Nullican (eds.) Chemcyclopedia. Washington, DC: American Chemical Society, 1988. , p. 219] **PEER REVIEWED**

ORMULATIONS/PREPARATIONS

March 12, 1991
Project No: 400754

APPENDIX H

Titanium Dioxide

Du Pont Environmental Remediation Services

TOXICITY SUMMARY

TiO_2

LIMITED DISTRIBUTION

This review reflects the available toxicity literature, both published and unpublished. Studies have not been evaluated for scientific merit.

*****

This report has been made available to you free of charge and at your request. We believe the information contained herein is reliable; however, we make no warranty, expressed or implied, and assume no liability in connection with any use of this information.

*****

Common Name:	Titanium dioxide (TiO_2)
Chemical Name:	Titanium oxide
Synonyms:	C. I. Pigment White 6 C. I. 77891 Hombitan® R Ti-Pure® R (rutile form) Ti-Pure® (anatase form) Unitane® Titanox®
CAS Registry No.:	13463-67-7
Chemical Structure:	O=Ti=O

Physical Properties: (1,17)

Description:	White solid, no odor
Molecular Weight:	79.9
Boiling Point:	2500-3000°C
Melting Point:	1830-1850°C
Specific Gravity:	3.9 (anatase) 4.23 (rutile)
Vapor Pressure:	--
Flash Point/Flammability:	Does not burn
Explosive Limits:	--
Solubility:	Insoluble in water, HCl, alcohol, or nitric acid Soluble in hot sulfuric acid, HF, or alkali
Conversion Factors:	--

This literature search contains 32 pages of text and 206 references.

This search was prepared by Marsha A. Lee. See the last page of this document for its updating history.

Exposure Standards:

AEL = 10 mg/m^3 (8-hour TWA, total dust; 5 mg/m^3 (8-hour TWA, respirable dust) (24).

ACGIH TLV = 10 mg/m^3, total dust (1)

OSHA PEL = 15 mg/m^3, total dust (16b)

OSHA TWA = 10 mg/m^3 - total dust (16b)

DOT Classification:

None

EPA RCRA Status:

No information is available.

40 CFR 415.220 - Environment protection, effluent guidelines and standards

FDA Status:

TiO_2 is cleared under Title 21 CFR for the following uses (16a):

Granted prior sanction for use in the manufacture of paper and paperboard products used in food packaging, and listed in §181.30.

Exempted from tolerance requirements under §182.99 (ADJUVANTS FOR PESTICIDE CHEMICALS) when used preharvest as a pigment/coloring agent in plastic bags to wrap growing bananas (FR July 2, 1981).

Cleared under §175.105 (ADHESIVES).

Cleared as an optional substance under §175.210 (ACRYLATE ESTER COPOLYMER COATING).

Cleared as a pigment and colorant under §175.300 (RESINOUS AND POLYMERIC COATINGS), §175.380 (XYLENE-FORMALDEHYDE RESINS CONDENSED WITH 4,4'-ISOPROPYLIDENEDIPHENOL EPICHLOROHYDRIN EPOXY RESINS), §175.390 (ZINC-SILICON DIOXIDE MATRIX COATINGS), §176.170 (COMPONENTS OF PAPER AND PAPERBOARD IN CONTACT WITH AQUEOUS AND FATTY FOODS), §177.1210 (CLOSURES WITH SEALING GASKETS FOR FOOD CONTAINERS), §177.1350 (ETHYLENE-VINYL ACETATE COPOLYMERS), AND §177.1460 (MELAMINE-FORMALDEHYDE RESINS IN MOLDED ARTICLES).

Cleared under §177.1200 (CELLOPHANE) and §177.1400 (WATER-INSOLUBLE HYDROXYETHYL CELLULOSE FILM).

Cleared as a substance employed in fiber finishing in the production of resin-bonded filters under §177.2260 (FILTERS, RESIN-BONDED).

Cleared in polysulfide polymer-polyepoxy resins for contact with dry food under §177.1650 (POLYSULFIDE POLYMER-POLYEPOXY RESINS).

Cleared as a filler and a color in the preparation of rubber articles under §177.2600 (RUBBER ARTICLES INTENDED FOR REPEATED USE). Total colors not to exceed 10% by weight of rubber product.

Cleared as an adjuvant substance employed in production of, or added to, textiles and textile fibers under §177.2800 (TEXTILES AND TEXTILE FIBERS).

Exempted from tolerance requirements under §582.99 (ADJUVANTS FOR PESTICIDE CHEMICALS) when used as a pigment/colorant in pesticide formulations for animal tags (FR January 23, 1985).

FDA tentative final Order would clear under §178.3297 (COLORANTS IN POLYMERS) (FR April 6, 1988).

USDA Meat and Poultry Inspection Division requirement that titanium dioxide be used as a marker at 1% in meat loaves, sausages and other meat products containing isolated soy protein and in isolated soy protein used in federally inspected poultry plants rescinded as of June 8, 1984 (FR April 17, 1970; FR May 9, 1984).

Petition withdrawn October 8, 1964, would have cleared titanium dioxide up to 0.1% by weight in tagged isolated soy protein used in processed meat products. FDA advised petitioner that the use is covered under the color additive law.

Petition withdrawn December 30, 1966, would have cleared rigid polyvinyl chloride sheeting colored with titanium dioxide.

Glastic Corporation petition October 27, 1964, would amend §177.2420 (UNSATURATED POLYESTER-STYRENE COPOLYMER RESINS) to clear titanium dioxide as a miscellaneous material.

USDA proposal February 21, 1969, would clear use to color canned ham salad spread, ham and cheese spreadable sandwich spread, and creamed wafer sliced beef and similar spread and creamed type products, at levels up to 0.5%.

Phillips Petroleum petition May 8, 1971, would clear use in combination with polyphenylene sulfide resins as coatings or components of articles intended for food-contact use.

FDA proposal April 6, 1988, would list "for use as a colorant only" under §176.170 (COMPONENTS OF PAPER AND PAPERBOARD IN CONTACT WITH AQUEOUS AND FATTY FOODS).

21 CFR 73.575; 21 CFR 73.1575; 21 CFR 73.2575 - Color additive certification.

51 FR 24815-24816 - Color additive, contact lenses.

21 CFR 177.2355(b) - Mineral reinforced nylon resins.

21 CFR 181.30 - Prior-sanctioned food packaging component.

TSCA Inventory:

Yes

TOXICITY

Summary:

Titanium dioxide (TiO_2) has very low acute oral toxicity with no deaths in rats given as much as 24 g/kg. Contact of the dry powder with the skin or eyes of rabbits did not produce significant irritation. Acute four-hour inhalation exposures of rats to TiO_2 produced no mortality at concentrations as high as 6.82 mg/L. Intratracheal administration also indicated a low level of acute toxicity. In a two-week inhalation study, rats exposed to 1.92 mg/L showed a typical dust-cell reaction. Only a typical dust-cell reaction was seen in rats exposed for four weeks to 1000 mg/m^3 and then held for up to one year. In a two-year oral bioassay, groups of 100 rats and mice each were given diets containing 2.5 or 5% TiO_2. Except for white feces, there were no clinical signs of toxicity seen. Tumor incidence was similar in the control, low-dose, and high-dose groups for both rats and mice. Under the conditions of this study, NCI concluded that TiO_2 was not carcinogenic in rats or mice. In the two-year inhalation study, groups of 100 male and 100 female rats were exposed six hours/day, five days/week to 10, 50, or 250 mg/m^3 of TiO_2, mostly of respirable size. Survival of the TiO_2-exposed rats was comparable to the controls. These TiO_2-exposed animals did not have any compound-related clinical signs of toxicity. Gross pathological examination revealed a dose-related increase in the amount of pigment in the lungs. Histopathological evaluation showed a significant dose-related increase over controls in the incidence of rhinitis, squamous metaplasia, and tracheitis. The incidence of benign and malignant lung tumors was also significantly increased in the high-dose group. These tumors included

bronchioloalveolar adenomas and epithelioid (squamous cell) carcinomas. Also seen were doserelated increases in pleurisy, collagenized fibrosis associated with cholesterol granulomas, alveoli bronchiolarization, pneumonia, and alveolar cell hyperplasia. The changes seen in the 10 mg/m^3 group were minimal in severity in comparison to similar effects seen in the controls (except that the alveolar cell hyperplasia was not seen in controls). These changes are reversible in nature. The degree of pulmonary fibrosis seen at the two higher doses was slight. TiO_2 has not shown any mutagenicity in Bacillus subtilis, in the Syrian hamster embryo cell bioassay, or the Ames test.

A. Acute

1. Oral

- A group of 20 guinea pigs and 16 rats was fed TiO_2 at doses of 300 to 24,000 mg/kg. One guinea pig fed 1500 mg/kg died of non-compound related causes. None of the other animals died. Two rats fed 24,000 and 16,000 mg/kg, respectively, showed some evidence of liver and kidney injury (17).

- Single oral doses of 1275 mg/kg TiO_2 were well tolerated by groups of rats and guinea pigs with no apparent adverse effects (24).

- Groups of six rats were given single oral doses of barium, bismuth, calcium, and lead titanate. None of the rats given doses up to 12,000 mg/kg died. At the higher dose levels, the rats were lethargic for the first few hours. Within 12 hours, soft stools were noted in some rats. Other findings on the high dosage levels were: reduced activity, temporary loss of appetite, and brownish-colored discharge from the nose and eyes. Rats appeared normal one month after the test (10).

- TiO_2 containing 0.5% mono- and bis-butyl phosphate was given to rats as a corn oil suspension. None of the rats died when fed the material at doses up to 25,000 mg/kg. Clinical signs of toxicity included diarrhea, wet perineal area, and weight loss for one to two days (24).

- A urea-formaldehyde resin containing 50% by weight of TiO_2 was not lethal to rats fed up to 25,000 mg/kg (24).

- LD50 (redwinged blackbirds) = 100 mg/kg (100).

2. Skin

- LD50 (rabbits) = > 10,000 mg/kg (96).

- Titanium dioxide as a powder and as a 28% saline paste produced no irritation on the intact, shaved skin of guinea pigs (24).

- The Chamber-Scarification Test was used to assess the irritancy of TiO_2 powder applied to the abraded skin of humans. The TiO_2 powder was applied at a concentration of 300 ug once daily for three days. This test material was classified as having low potential irritancy to the skin (36).

- Six male albino rabbits with clipped hair received 0.5 g solid TiO_2 on their intact skin. The patches were covered for 24 hours; observations were also made at 48 hours. TiO_2 produced very slight skin irritation on 2/6 rabbits in 24 hours and no skin irritation in 48 hours (24).

- A patch test was done on 210 people using an elastomer staple containing 5% TiO_2 and 5% Daktose® B. No irritation or sensitization was seen in any of the subjects (24).

- No skin irritation was observed when TiO_2 was tested on the shaved, intact skin of six rabbits. Although no dermatitis hazard was expected, good industrial hygiene practice would call for prompt, thorough washing of the skin in case of exposure (24).

3. Eyes

- TiO_2 containing 0.5% of mono- and bis-butyl phosphate produced only temporary mild or minimal conjunctival irritation with no significant corneal or iritic effect when instilled as a solid or as a 10% propylene glycol suspension into the eyes of rabbits (24).

- TiO_2 has been introduced by tatooing into the cornea of rabbits and patients having corneal scars. TiO_2 has caused permanent white coloration but no irritation (44).

- Titanium dioxide with 2% antimony oxide caused temporary slight corneal opacity, transient minimal iritis, and very mild conjunctivitis when tested in a rabbit eye. The ocular effects were reversible, and the eye was normal within three days except for mild conjunctival redness which persisted through the three days. The eye treated with the compound and promptly washed had no ocular effects. Titanium dioxide with 2% antimony oxide micronized with 0.3% triethanolamine and with 3.7% antimony oxide micronized with 0.3% triethanolamine caused localized areas of transient slight opacity and very slight conjunctival irritation with no iritic effect in unwashed and washed rabbit eyes. All eyes were normal within one to two days (24).

4. Inhalation

- After controlled inhalation of TiO_2 by rats, the distribution of dust retained in the tissues was studied. TiO_2 was eliminated bronchially with less than 10% of the originally retained dust collecting in the lymph nodes (57).

- Rats were exposed to an aerosol of either anatase or rutile, and the retention time in the lung was determined up to 132 days post-exposure. Particle clearance from the lung was similar in both anatase and rutile with half-times of 51 or 53 days, respectively. Additionally, a pulmonary cell response test was done with other rats. After intratracheal instillation of anatase and rutile in doses of 0.5 or 5.0 mg/rat, lung lavage was done and the harvested cells counted and compared. The results for count and type of cell were similar for both types of TiO_2. Both anatase and rutile are labeled "nuisance" dusts (32).

- Under aseptic conditions, 25 or 50 mg TiO_2 suspended in 0.4 cm^3 aqueous NaCl was introduced into the trachea of rats. After three or six months of observation, the animals were killed and their lungs were separated to determine their weight, action and immunological properties. TiO_2 reduced the breathing amplitude and increased the sensitivity to histamine introduced into the pulmonary artery. The weight of the lungs was 60% higher than that of the control group. TiO_2 reduced the elimination of antigen molecules by lung and liver macrophages (92).

- Male mice were intratracheally instilled with 11.8 ug of TiO_2 or phosphate buffer solution. Animal sacrifices were done at 15 minutes, 1, 5, and 20 hours, and three and seven days post-exposure. Bronchopulmonary lavage was done on three mice from each group. The mice from both groups appeared normal throughout the study; 15 minutes after instillation, TiO_2-treated mice retained 66% of the administered dose (33).

- Morphological changes were observed after three months in the lungs and lymphatic nodes of male rats intratracheally given a single dose of 25 or 50 mg TiO_2. Marked damage to the pulmonary alveoli, both mechanical and functional, occurred. Morphological changes in the pulmonary parenchyma were associated with increased activity of succinic dehydrogenase, lactic dehydrogenase, beta-hydroxybutyric dehydrogenase, ATPase, and acid phosphatase, but a reduced activity of alkali phosphatase. Histochemical changes noted in lymphatic nodes were manifested by a strong activity of succinic dehydrogenase and phosphatases. No important morphological or histochemical changes were seen in the spleen; no changes were seen in the amount or localization of lipids in the organs (51).

- Guinea pigs were exposed to TiO_2 aerosol housed in a stainless steel chamber. The lungs were lavaged, and the free cells were counted. The number of macrophages present increased in the TiO_2 inhalation group relative to controls. The number of leukocytes were equal for both groups (97).

- Female rats were exposed for 10 minutes to white smoke generated from a mixture of TiO_2-hexachloroethane (HC) in an inhalation chamber operated in the static mode. The dose was varied by varying the amount of smoke mixture and/or the exposure time. The titanium concentration was in the range of 2.5-5.0 g of the smoke mixture; TiO_2 = 29% (w/w) of the mixture, HC = 59.1%. The particle size increased with the smoke concentration and time. All animals survived. The smoke was irritating to the eyes and nasal mucous membranes, and during exposure, the rats were restless and kept their eyes closed. After exposure, rats exposed to the highest concentration of smoke had wet noses, nasal discharge, and swollen eyelids. Symptoms decreased gradually, and within 24-48 hours, the rats appeared normal except for those at the highest concentration. The eyelids of these rats were swollen for a one-week observation period. The lungs showed no gross changes. In microscopic findings, most rats had discrete lung changes with localized interstitial pneumonitis with a sparse admixture of granulocytes and mononuclear cells. Also mild bronchioloalveolar hyperplasia and increased numbers of lymphocytes and eosinophilic granulocytes around vessels and bronchi appeared.

  Forty-two rats exposed for 10 minutes to 7 g TiO_2-HC smoke were sacrificed at varying periods up to three months after exposure. None died and there was a normal lung gross appearance. Histological examination in the first three days showed edema and small inflammatory changes. One to two weeks after exposure, small localized atelectases with collapsed alveoli, septal proliferation and sparse admixture of inflammatory cells were evident (56).

- The Approximate Lethal Concentration of titanium dioxide with 2% antimony oxide micronized with 0.3% triethanolamine is greater than 2.28 mg/L (male ChR-CD® rats, exposed head-only for four hours). The mass median diameter of particles generated was 1.50 to 1.75 microns (24).

- The Approximate Lethal Concentration of titanium dioxide with 2% antimony oxide in male rats exposed (head only) for four hours is greater than 3.56 mg/L (the highest test concentration practical). Particles tested had a mass median diameter of 1.85 to 2.80 microns (24).

- When ChR-CD® male albino rats were exposed head only for four hours at concentrations up to 6.82 mg/L of titanium dioxide (with 3.7% antimony oxide micronized with 0.3% triethanolamine), no mortalities were produced. The Approximate Lethal Concentration of the test material is greater than 6.82 mg/L (particles with a mass median diameter of 1.55-1.70 microns). Generation of time-weighted average chamber concentrations greater than 6.82 mg/L was not practical under our test conditions (24).

- Four-month old MRC female rats were instilled with 0.25, 0.5, 1.0, or 5.0 mg of TiO_2 in saline solution. After four weeks, the treated rats were sacrificed, and the lungs were removed. The lungs were lavaged with 0.15 M saline. A count of free cells was done on the total lavage fluid from all animals. The 5.0 mg TiO_2-treated animals had elevated cell numbers; however, the amount may not be statistically significant. Acid RNase levels were equal between TiO_2-treated rats and controls. DNA per gram of lung tissue in the 1.0 and 5.0 mg TiO_2 groups increased relative to controls. The TiO_2-treated rats also exhibited a large amount of free dust particles in the lavage fluid (93).

- Thirty rats were lightly anesthetized with ether. One mL of a 5% saline suspension of TiO_2 was injected into the trachea of 15 of the rats and 1 mL of saline was injected into the trachea of the 15 controls. None of the rats died, and no clinical signs of toxicity were noted. Gross or histopathological examination did not reveal any adverse changes (24).

- Rats were given 0.25 mL of a 1% saline suspension of TiO_2 by intratracheal administration. Five rats were sacrificed on days 2, 7, 27, 90, 182, and 371 post-exposure for histopathological examination. Following intratracheal injection of the test material, transitory acute bronchiolitis and peribronchiolar pneumonia were recognized. Subsequently, collagenized granulomas developed in the dust-deposited bronchiolar and adjoining alveolar walls by the sixth month post-exposure. At one year post-exposure, moderately collagenized fibrotic scars remained in the dust-deposited areas. The test material was considered to be a slightly fibrogenic fiber (24).

- Rats were given 50 mg of TiO_2 intratracheally. TiO_2 caused no nodule formulation in lung tissue, and only dark-colored dust deposits were observed. However, in one case, there were traces of macrophage infiltration in the alveoli and in another, incipient diffuse fibrosis (43).

- The injection of TiO_2 dust into the rabbit lung resulted in diminished lung ventilation one week after treatment. Pronounced intraalveolar dust cell reactions were revealed with some thickening of the alveolar walls. The lungs had returned to normal three months after the treatment (18).

- The double introduction of 50 mg of TiO_2 into the lungs of rats failed to produce a sclerotic process (76).

- CD rats were exposed to aerosols of TiO_2 for six hours or three days at a concentration of 100 mg/m^3. Time-course studies were done at 0, 24, 48 hours, eight days, and one month after exposure. Results showed that TiO_2 produced no alterations in biochemical, cytochemical, or functional parameters resulting from broncho-alveolar lavage (118).

- TiO_2, 50 mg in 0.5 mL of saline, was administered to rats intratracheally. No clinical symptoms were observed in the course of eight to 11 months after treatment. After this period, the rats were killed and their lungs examined histologically. Some infiltration and sclerotic changes were found but without tending to granuloma formation (74).

- Experimental evaluation of the fibrogenetic power of TiO_2 dust showed little reaction. The response was determined by lung weight, macro- and microscopic appearance, and detection of L-hydroxyproline (108).

- One mL of a 5% saline suspension of TiO_2 containing either 1% Al_2O_3 or 1% Al_2O_3 and 1% Sb_2O_3 was injected intratracheally directly into the lungs of groups of four rats. All rats survived the injection but showed evidence of immediate respiratory difficulty. Thereafter, all the rats showed normal respiration and normal rate of weight gain. Histological examination revealed an increase in lung weight and slight to moderate focal cellular changes in the group given the Sb_2O_3-containing pigment. The rats given the Al_2O_3-containing pigment showed minimal lung changes (24).

- Rats were given a TiO_2 pigment containing 13% SiO_2 and 1% Al_2O_3 by intratracheal injection. Administration of the TiO_2 sample at levels up to and including 600 mg/kg did not kill the rats or affect their rate of weight gain over a two-month period. Histological examination revealed a response typical of a physiologically inert foreign body (24).

- Intratracheal administration of a urea-formaldehyde resin containing 50% by weight of TiO_2 to young rats did not produce any significant clinical signs or pathological effects. The lung tissue gave only a typical foreign body response (24).

- Intratracheal administration of TiO_2 gave no histological evidence of any fibrous processes. Similar administration of SiO_2-TiO_2 mixtures caused lung changes which were dependent on the SiO_2 content (120).

- Introduction of TiO_2 into the respiratory tract of white rats showed, after four months, an accumulation of cells around dust particles in the lungs as well as around the bronchi and vessels. Later, these cell accumulations were traversed by fibers of the connective tissue (77).

- Male Wistar rats were injected intrapleurally with TiO_2 of particle size 0.8-12.7 um (dose not specified). No pleural effusion was observed in rats killed one or two days after treatment, but numerous small (1-2 mm) whitish plaques were seen scattered irregularly on the visceral and parietal pleurae. Numerous black granules were seen extracellularly and within macrophages. After one week, all the particles of the injected material were seen to be within macrophages which were clustered together forming small or large plaques attached to the pleura. There was no further change in the histological picture one or three months after treatment, but a few strands of connective tissue were seen surrounding the macrophage collections or within the collection of macrophages. The lymph nodes draining the injection site contained a variable number of macrophages full of black granules (45).

- Intratracheal injection of 20 mg of TiO_2 had no effect on the general condition or weight gain of rats. Lymph node weights were significantly higher in the TiO_2 group than in the controls (42).

- A study of L fumes generated from the manual metal arc (MMA) welding of mild steel with a Lime electrode and S fumes generated from the MMA welding of stainless steel with a Lime-titania electrode was done in rats. The eight rats in each group were exposed to 1000 mg/m^3 fumes for one hour in the single exposure study. The total number of welding operations during the exposure period was 23 for the L electrode and 20 for the S electrode. The very small welding particles tended to aggregate into larger, coherent masses. TiO_2 comprised 0.25% of the fumes from the L electrode and 11.47% from the S electrode. No deaths were seen and no marked changes were observed during the 14-day recovery period. Macroscopic abnormalities were seen: on the second day, the gross color of the lungs of both groups was dark red, and gray pigmented spots were found randomly distributed. The degree of these changes was slightly lower for L fumes than for S fumes. On the seventh day, these changes were gradually recovering. On the 14th day, the lungs from the L fumes-exposed rats were normal, whereas slight damage

was still seen in the S fumes-exposed rats. Histopathologically, on the second day, yellowish-brown granules appeared in the respiratory bronchioles, alveolar ducts and alveoli and alveolar macrophages. A hyperplasia of mucus cells in the bronchial epithelium was seen more in the S than in the L fumes-exposed rats. The hyperplasia of mucus cells in the lungs of the S fumes-exposed rats was slightly more severe on the seventh day than the second day, whereas, this lesion was nearly absent in the L fumes-exposed rats. On the 14th day, the S fumes-exposed rats still contained these lesions (113).

- Rats inhaling 15.5 mg TiO_2/m^3 for seven hours resulted in deposition of up to 179 ug TiO_2 per lung. TiO_2 appears to accumulate extensively within the rat body and lungs when inhaled, although some clearance of the compound from the rat lung is demonstrated. A substantial portion of inhaled TiO_2 was cleared from the lungs by retrograde ciliary movement during the 7-hour inhalation period in rats. Over a 25-day period after exposure, TiO_2 levels decreased from 179 ug/lung to about 110 ug/lung. Fifty percent of the deposited TiO_2 was cleared by 31-32 days, while the remaining 50% was retained in the lungs (99).

5. Injection Studies

a) Intraperitoneal

- Intraperitoneal injection of 2.0 mL of a 5% TiO_2 suspension in saline showed no signs of toxicity in guinea pigs (24).

- Intraperitoneal injection of 0.5, 2.0, 6.0, or 15.0 mg of TiO_2 did not cause any fibrotic reaction in rats (43).

- Rats and mice were injected with 10 mg and 2.5 mg, respectively, of TiO_2. There was no significant effect seen on splenocyte mitogenesis (48).

- Male Wistar rats were injected with anatase TiO_2 (dose not specified) of particle size 0.8-12.7 um. The reaction consisted of collections of macrophages surrounded by a thin layer of fibrous tissue. Black granules, presumed to be TiO_2, were found in abdominal lymph nodes and in Kupffer cells (45).

- The acute intraperitoneal LD50's of barium, bismuth, calcium, and lead titanate were determined to be 3000, 2000, 5300, 2000 mg/kg, respectively (10).

- No acute poisonous effects were observed in mice given a single intraperitoneal injection (5 mg) of TiO_2-containing pigments (T1-T6). Phagocytic activity of the peritoneal cells revealed some differences between groups. Group T1 gave a fairly low

response two days after injections, but the silica-rich pigment (T3) reacted faster and did not change much during the whole experiment. In further studies (T2, T4, T5, T6), the phagocytosis of pigment particles resulted in a higher uptake than in the T1 and T3 groups. The average amount of pigment-loaded cells varied from approximately 25-50% in two to 15 days. The intraperitoneal administration of TiO_2 pigments to mice increased the cell number in the peritoneal cavity time dependently in the control and the T1 and T3 groups. The activity of beta-glucuronidase in the peritoneal phagocytes did not show as much variation as acid phosphatase in the same cells (87).

- Male and female Swiss mice were given single 1 mL intraperitoneal injections of 1% of Ti-Pure®. Leukocytes were collected from the peritoneal cavity, peripheral blood leukocytes were collected from the tail veins, and bone marrow cells were collected from the femurs. There was an increase in the number of monocytes at 24 hours in peripheral blood (to 539/mm^3). The numbers of peripheral blood and peritoneal lymphocytes and granulocytes stayed within normal ranges during the reaction period (115).

b) Intravenous

- No information is available.

c) Subcutaneous

- Guinea pigs were injected with 25 mg of TiO_2. No signs of abscess formation were seen (105).

B. Extended Studies

1. Oral

- TiO_2 was fed to 30 rats for 13 days at 0.25% of their diet. The feces collected from the seventh to thirteenth days were analyzed for TiO_2. The average recovery was 92% of the amount fed (67).

- Rats were fed 660 mg/kg TiO_2 for 15 days. No Ti was found in the blood, liver, kidney, or urine (35).

- Two groups of ten male and ten female rats were fed 10% TiO_2 in their diets for 30-34 days. All animals remained healthy and normal. No relevant gross pathology was observed (2).

- Three groups of two dogs were given 50, 100, or 150 mg of TiO_2. Every five days the dose was increased by the same amount. One dog of each group was studied for one month, the other for two months. No toxic effects were seen (116).

- TiO_2 was fed to sheep in amounts as large as 2-3 g/day for as long as three months without any ill effects. The TiO_2 was completely excreted in the feces (4).

- When rats were fed 1.28, 2.57, or 3.21 mg TiO_2/day for five months (a close equivalent to that consumed by a person eating 150 g/day of cheese containing 0.2-0.5% of this food-bleaching agent), alternating maximum and minimum of accumulation in the liver and kidney and excretion in the feces were noted. This was especially marked with the two higher doses. Similar results were obtained when the compound fed was $TiCl_3$ (3.21 mg/day). Ti was not found in the liver and kidneys during approximately the first month of TiO_2 or $TiCl_3$ feeding (85).

- F-344 rats were fed diets containing 0, 1, 2, or 5% TiO_2-coated mica for up to 130 weeks. No consistent or biologically important changes in survival, body weight gains, or hematologic or clinical chemistry parameters were noted. Ophthalmoscopic exams during week 104 revealed a dose-related increase in the incidence of cataracts in male but not female rats. However, the incidences of microscopic cataracts were similar in all groups of rats. The high dose of TiO_2-coated mica was associated with a slightly increased incidence of adrenal medullary hyperplasia in males, but there was no evidence of progression of this change to either benign or malignant pheochromocytoma; also there was no evidence of an adrenal medullary proliferative response in females. The incidence of mononuclear cell leukemia was elevated in high-dose males that survived to termination, but there was no evidence that the TiO_2-coated mica either induced or hastened the onset of the disease (8).

- Two guinea pigs, two rabbits, two cats, and one dog were fed TiO_2 for 390 days. The dog received 9 g/day, rabbits and cats received 3 g/day, and guinea pigs got 0.6 g/day. Two additional cats received 3 g of pigment daily for 175 and 300 days, respectively. A number of internal organs were analyzed for titanium, including the liver and the kidney. No evidence of titanium was found. This negative finding of titanium in the internal organs, coupled with an absence of toxic signs and gross or micropathological organ changes led to the conclusion that TiO_2 acts as an inert substance (64).

- Groups of 50 Fischer 344 rats of each sex and 50 B6C3F1 mice of each sex were given TiO_2 in the diet at either 25,000 or 50,000 ppm for 103 weeks and then observed for one additional week. Matched controls consisted of 50 untreated rats or each sex and 50 untreated mice of each sex. All surviving rats and mice were killed at 104 weeks.

Administration of the TiO_2 had no appreciable effect on the mean body weights of rats or mice of either sex. With the exception of white feces, there was no other clinical sign that was judged to be related to the administration of TiO_2. Survival of the rats and the male mice at the end of the bioassay was not affected by the test chemical; mortality in female mice was dose related. Sufficient numbers of dosed and control rats and mice of each sex were at risk for development of late-appearing tumors.

In the female rats, C-cell adenomas or carcinomas of the thyroid occurred at incidences that were dose related ($P = 0.013$), but were not high enough ($P = 0.043$) for direct comparison of the high-dose group with the control group to meet the level of $P = 0.025$ required by the Bonferroni criterion (controls 1/48, low-dose 0/47, high-dose 6/44). Thus, these tumors of the thyroid were not considered to be related to the administration of TiO_2.

In the male and female mice, no tumors occurred in dosed groups at incidences that were significantly higher than those for corresponding control groups (83).

2. Inhalation

- Groups of male albino rats were exposed (head only) to TiO_2-coated dust particles (1.92 mg/L). Rats were treated six hours/day, five days/week for two weeks. Gross and histopathological examinations were done at the end of the study. Absolute lung weights increased slightly (24).

- Two groups of eight male rats each were exposed to L fumes from the manual metal arc (MMA) welding of mild steel with a Lime electrode and S fumes generated from the MMA welding of stainless steel with a Lime-titania electrode. The rats were exposed to 400 mg/m^3 fumes for 30 minutes/day, six days/week, for two weeks. The total number of welding operations during the exposure period was 10-12 daily for both electrodes. TiO_2 comprised 0.25% of the fumes from the Lime electrode and 11.47% from the Lime-titania electrode. No marked changes were seen during the treatment period in general symptoms, behavior, respiration, or feces. The results of hematologic and serum-biochemical analysis and urinalysis was comparable to the controls. Gross examination at autopsy showed a dark-red coloration of the lungs of all the S fumes-exposed rats. Weights of the other organs were normal, while the wet weight and relative lung weights of the L fumes- or S fumes-exposed group increased to approximately 1.2 times and 1.7 times those of the controls.

Lungs from the L or S fumes-exposed rats contained yellowish-brown granules and macrophages; the numbers of granules being less in the S fumes than the L fumes. However, in S fumes-exposed rats, large numbers of pink granules were seen outside macrophages in the alveoli. Some bronchial lesions such as hyperplasia of mucus cells in the epithelium and bronchiectasia were seen in the lungs from the S fumes but not in those from L fumes (113).

- Rats were exposed to 0 or 1.9 mg/L of silica-coated TiO_2 for two weeks. Rats were killed 0, 1, 3, 6, and 12 months post-exposure. After the rats were exposed for two weeks, their pulmonary response to silica-coated TiO_2 was characterized by dust-laden macrophage (dust cell) response with hyperplasia of type II pneumocytes. After the rats were exposed for three months, foamy macrophage infiltration in silica-coated TiO_2 was evident. By six months post-exposure, the lung was restored to essentially normal architecture with removal of most dust cells. After one year post exposure, the lungs were almost normal with only a few dust cell aggregates remaining (62).

- Female guinea pigs were exposed for 14 days (20 hours/day) to an aerosol of TiO_2 dust (rutile crystal lattice) to produce a macrophage blockade. Then the animals were infected by aerosol with Legionella pneumophila. The findings indicated that the lattice form of rutile was inert, nonfibrogenic, and did not induce pathological changes in the lungs. However, the dust particles did persist and even six weeks after exposure, large numbers of dust-laden pulmonary macrophages remained in alveoli, airways, and pulmonary lymphoid tissue. Alveolar wall thickening occurred on a small scale, due to the accumulation of macrophages in the interstitium and not to deposition of connective tissue fibers. Extracellular TiO_2 particles were still found at six weeks, probably representing dust released from lysed macrophages. The macrophage blockade did not change the susceptibility of the animals to Legionnaires' Disease nor did it increase mortality. In the early stages, the blockade limited multiplication of L. pneumophila in the lungs. Later blood monocytes were recruited into the lungs where they phagocytosed L. pneumophila, resulting in lung counts which were comparable to those of the controls (6).

- Fifteen guinea pigs were exposed eight hours/day, five days/week for three weeks to 24 mg/m^3 of TiO_2 dust and examined four, eight, 16, and 23 weeks later. Body weight or lung weight was not affected. Lymphocytes and neutrophils were not increased at 16 and 23 weeks after exposure. A slight but non-significant increase in the phagocytosis capacity was found four and eight weeks after exposure. Enzyme production was unchanged (34).

- Inhalation of TiO_2 dust by animals (species not stated), eight hours/day for 30 days caused no appreciable disturbance of health (116).

- Rats were exposed (whole-body) to a dust atmosphere of TiO_2 (10 mg/m^3) for seven hours/day, five days/ week, for 1, 2, 4, 8, and 12 weeks and then sacrificed. Another group of animals were exposed for 12 weeks and held for 12 months before sacrifice. It was found that alveolar macrophages contained variable numbers of dust particles throughout all exposure periods and were confined to the airspaces. There was no significant change noted in the differential cell count of alveolar-free cells. The percentage of alveolar macrophages was in excess of 96%. The rest of the cells were polymorphonuclear leukocytes and lymphocytes. A few dust-laden cells were found in the interstitium after 12 weeks of dusting. Pleural fibrosis was widespread after 12 weeks of exposure and 12 months of recovery (53).

- In a study of the effects of coalmine-dust exposure on bronchoalveolar leukocyte concentration, TiO_2 was a comparison dust administered to male, syngeneic rats at 10 or 50 mg/m^3 for 2, 4, 8, 16, 32, or 75 days. Results showed that TiO_2 exposure only caused inflammation at the end of the 50 mg/m^3 exposure. TiO_2-exposed rat leukocytes behaved like those from controls (21).

- Exposure of mice for several weeks to an inert, particulate aerosol of TiO_2 at a respirable aerosol concentration of 20 mg/m^3 impaired the clearance of Pasteurella haemolytica in proportion to the duration of exposure. Other groups exposed to a lower respirable concentration of 2 mg/m^3 showed similar clearance rates relative to control mice. A recovery experiment showed that inhalation of TiO_2 at 20 mg/m^3 for 10 days impaired bacterial clearance at least 10 days after cessation of exposure to TiO_2 (40). Additionally, lymphocytes from the mediastinal lymph nodes had depressed responses to bacterial antigen in vitro in the mice (41).

- In a range-finding study, rats were exposed six hours/day, five days/week for four weeks to 1000 mg/m^3 of TiO_2. After the exposure period ended, the rats were observed for up to one year. Clinical and pathological findings were indicative of a typical dust cell reaction (24).

- Male and female rats were exposed six hours/day, five days/week for 12 weeks to 15.95 mg/m^3 of TiO_2 dust. This exposure caused no noticeable changes in appearance, behavior, or body weight. Tumor incidence was not different from normal incidences in this species of rat (111).

- TiO_2 administered intratracheally to 48 hamsters at a maximum dose of 3 mg/application once a week for 15 weeks induced interstitial cell proliferation, bronchial epithelial alterations, and a few granulomatous changes in the pulmonary system, but no tumors (106).

- Twenty-eight guinea pigs were subjected to high concentrations of TiO_2 dust. Various groups of these animals were exposed for periods ranging from two hours to four months. Pathological examination of the lung tissue indicated that TiO_2 penetrates deeply, causing an inflammatory reaction which continues for some time. The pathological change noted resembled those caused by exposure to pneumoconiosis-producing dusts. Pneumoconiosis due to "inert" dust should be distinguished from silicosis produced by silica dust which stimulates the growth of interstitial tissue. This work indicates that even an "inert" dust may be harmful if a sufficiently large amount is inhaled (65).

- Rats were exposed to a TiO_2 dust at 0, 3.2, 8, or 20 mg/m^3 for eight months. The rats were sacrificed, and their respiratory tissues examined histopathologically. The rats showed accumulation of particles on the bronchial and peribronchial tissues, including the lymph nodes. Aggregation and accumulation of particle-laden macrophages and infiltration mononuclear cells were seen. Hyperplasia and hypertrophy of epithelial cells associated with septal thickening were noted. Accumulation of TiO_2 in all upper respiratory tissues was sporadic and produced no observable effects (110).

- When inhaled at 40-60 mg/m^3 by rats for one to 12 months, TiO_2 aerosols caused desquamation of the lung tissue, interstitial coniosis, bronchitis, and emphysema (98).

- Dogs were exposed intratracheally to TiO_2 dust for 9-15 months. Examination showed the dust to be nearly pure titanium. Dust in the lung deposited mainly in the respiratory bronchioles and adjacent alveoli, with many alveoli filled by compacted dust particles. The pulmonary responses consisted of slight alveolitis, centrilobular emphysema, focal collapse of alveoli, and fibroblast hyperplasia with a few collagen fibers surrounding some of the TiO_2-dust foci. Many alveolar macrophages with intact nuclei contained a great amount of dust particles in the lysosomes; in the dust foci, most of type I pneumocytes disappeared, and type I pneumocytes showed hyperplasia. The alveolar subepithelial basement membrane was markedly thickened, and bundles of collagen fibers were formed in the interstice (123).

- In bronchoalveolar lavage fluid from rats and Syrian golden hamsters exposed for one year to fly ash from a power plant, TiO_2, or diesel engine exhaust gases, the activities of lactate dehydrogenase, alkali phosphatase, and acid proteinase, and the concentration of total protein were above normal. Leukocyte number in the fluid increased after exposure to the three components. Macrophage and granulocyte number decreased after exposure to fly ash or TiO_2 (81).

- Rats were exposed to dusty atmospheres containing TiO_2 (43-328 mppcf) for as long as 13 months. No differences in weight between control and experimental rats were evident. The inorganic content of the lung increased showing retention of TiO_2. Microscopic examination showed that TiO_2 apparently reached the alveoli and alveolar ducts. Here the pigment remained in the intracellular position within macrophages; there was only slight lymphoid proliferation in these areas. No other reactions were noted in the lungs, even after 20 months (15).

- One hundred male and 100 female rats were exposed six hours/day, five days/week for up to two years to 0, 10, 50, or 250 mg TiO_2/m^3, the majority of which was of respirable size. Lower mean body weights, higher incidences of irregular respiration, abnormal lung noises, and stained and wet perineum were the gross clinical observations. Gross pathological and histopathological examinations of exposed rats revealed that TiO_2 accumulated within the upper respiratory tract airways, lungs, gastrointestinal tract, lymphatic system, liver, and spleen. The incidences of pneumonia, chronic traceitis, rhinitis with squamous metaplasia in the anterior nasal cavity, and retinopathy were increased slightly in all exposure groups. Dose- and time-dependent TiO_2 deposition and lung tissue responses to these deposits were seen. These tissue responses were characterized by lung weights that ranged as high as 3.4-fold heavier for rats in the 250 mg/m^3 treatment group than in the controls and more pronounced in females than in male rats.

  The microscopic tissue responses to TiO_2 were from the increased activity of the normal lung defense and clearance mechanisms. Most of the TiO_2 particles were localized within the alveolar macrophages. Neutrophilia was observed in exposed rats which aggregated within the alveolar ducts and adjoining alveoli with time. Associated with these cell clusters were the further thickened alveolar and alveolar duct walls resulting from Type II pneumocyte hyperplasia and bronchiolarization of alveolar cells.

  These lung cell responses are reversible, but continued exposure to and deposition of TiO_2 within the lungs were associated with dose-related alveolar proteinosis, cholesterol granuloma formation, focal pleurisy, and collagenized fibrosis. Lung tumor

formation was associated with, but not linked causally to the cellular responses to TiO_2. The incidence of bronchioalveolar adenoma, although seen in the control, 10 and 50 mg/m^3 groups, was significantly greater in the 250 mg/m^3 group. Cystic keratinizing squamous cell carcinomas were seen in rats exposed to the high-dose group. Adenoma rates were similar for male and females; however, cystic keratinizing squamous cell carcinomas were seen more among females. The biological responses of TiO_2 were more pronounced in female rats than in males.

The no-observable-effect level (NOEL) for the tumorigenic response and polycythemia was 50 mg/m^3. The NOEL for fibrosis, cholesterol granuloma formation, and alveolar proteinosis was 10 mg/m^3 (24v). The authors conclude that the test findings do not suggest that existing manufacturing practices in the TiO_2 industry or use by customers pose a risk of adverse health effects (112).

- Papers written based on the above two-year study discuss the effects of the lung responses. Potential adverse health effects appear to be negligible since there was no tissue response to translocated particles of TiO_2 in the lymph nodes, spleen, or liver (61). Also the lung tumors in the rats were different from common human lung cancers in terms of tumor type, anatomical location and tumorigenesis, and were devoid of tumor metastasis. Therefore, the biological relevance of these lung tumors and other pulmonary lesions for man is negligible (60,63).

- Male, Wistar rats were exposed to respirable fractions of TiO_2 at concentrations of 1-90 mg/m^3 for seven hours/day, five days/week, for 222 or 684 days. The rats were killed at various times up to 38 days after the last exposure. Data were fit to a kinetic model for deposition and clearance. Lung burden increased linearly with exposure time, except for a nonlinear phase occurring early in the exposure period. No TiO_2 was detected in lymph nodes at low-lung dust burdens. Lymph-dust burdens did not significantly increase until a substantial increase in lung burden occurred (117).

- The effects of mixed dust exposure on pulmonary clearance during chronic exposure was studied in rats exposed to combinations of quartz (at respirable dust concentrations of 1 and 10 mg/m^3) plus TiO_2, (at 30 and 20 mg/m^3, respectively), and amosite asbestos (2.5 mg/m^3) plus TiO_2 (15 mg/m^3). The rats were exposed for five days/week, for up to 16 weeks (quartz) or up to 32 weeks (asbestos). There was an absence of significant differences between the lung burdens (and 3, 10, and 38 days post-exposure) for single-dust and mixed-dust exposures. There was, however, some reduction in the post-exposure clearance (as shown by the lung burdens at 94, 150, and 260 days post exposure) of TiO_2 which appeared to be due to the presence of quartz in the lung. Transfer to lymph nodes accounted for most of the post-exposure clearance for TiO_2 and almost all for the quartz (73).

- Pooled rat lung tissue from male and female rats exposed to TiO_2 by inhalation at 0, 10, 50, and 250 mg/m^3 was analyzed for TiO_2 concentrations at 3, 6, 12, and 24 month sacrifice time-intervals. The tissues were analyzed on a dry weight basis after digestion in hydrofluoric acid. Aqueous aliquots of the digest were analyzed by inductively coupled plasma spectroscopy. Analysis shows that the amount that accumulates is proportional to the dose administered (24).

- See Related References 124-142 for more information.

3. Injection Studies

a) Subcutaneous

- Three dogs received weekly injections of a suspension of TiO_2 in oil. The initial dose of 500 mg was raised progressively to 3 grams over seven weeks. A fourth dog initially received 250 mg/kg rising to 2000 mg/kg. Three dogs survived without adverse effects; the fourth died of a cause unconnected with the administration of TiO_2 (116).

b) Intramuscular

- TiO_2 induced fibrosarcomas in three out of 50 rats given a single intramuscular injection in the thigh muscle (37). In a later communication, the author stated that he considered TiO_2 to be noncarcinogenic based on this experiment (38).

- Rats were injected daily to a dosage level of 360 or 260 mg/kg for two years (82).

c) Intraperitoneal

- Thirty-two male Marsh-Buffalo mice each received a saline suspension of 25 mg TiO_2 intraperitoneally; four neoplasms appeared over the 18-month study period. During this time, four neoplasms also appeared in 30 control mice receiving isotonic saline by the same injection route. A nonsignificant association of tumorigenesis with experimental treatment indicated a lack of carcinogenic tissue reaction in the mice that received the TiO_2. Focal deposits of dose material rather than a diffuse distribution were found on the intraperitoneal walls and muscles as well as the gut. In some instances, TiO_2 had migrated from the initial injection site. Mostly no foreign-body reaction to TiO_2 involving the presence of macrophages or capsular connective tissue formation was seen, although a dose deposit attached to the peritoneum by a transparent membrane was seen. In one mouse, chronic myositis developed in muscle tissue containing a large amount of dose material (9).

C. Carcinogenic Potential

- TiO_2 was not carcinogenic in a two-year oral study with Fischer 344 rats and B6C3F1 mice receiving diets containing 2.5 or 5% TiO_2. With the exception of white feces, there were no clinical signs of toxicity seen (83,84).

- In a two-year inhalation study, the incidence of benign and malignant lung tumors was significantly increased in rats exposed to 250 mg/m^3 of TiO_2. These tumors included bronchioloalveolar adenomas and epithelioid (squamous cell) carcinomas. At the lower concentrations in this study (10 and 50 mg/m^3), no increase in the incidence of tumors normally seen in this species of rat was observed (24).

- See Related References 143-147 for more information.

D. Mutagenic Potential

- TiO_2 gave negative results in the recombination-repair-deficient (Rec) assay using Bacillus subtilis to check for the material's DNA damaging capacity and mutagenicity (55).

- TiO_2 was tested for its capacity to enhance transformation of Syrian hamster embryo cells by a simian adenovirus, SA7. Chemical dilutions were added to mass cultures of hamster embryo cells 19 hours before or five hours after addition of SA7. The virus was absorbed for three hours, and the cells transferred for survival (500 to 700 cells/dish) and for the transformation assays (200,000 to 300,000 cells/dish). TiO_2 did not enhance the virus transformation even at a concentration of 12.5 mM (11,12).

- TiO_2 was neither toxic nor static in vitro when tested in Chinese hamster V79 cells (68).

- Bacillus subtilis strains H17 and M45 were tested for mutagenicity. Results with TiO_2 were negative (54).

- Titanium dioxide is nonmutagenic in the Ames assay using Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, and TA1538 without activation and with Aroclor®-induced rat liver S-9 (23,122). TiO_2 is also nonmutagenic in Escherichia coli (23). Another paper describes the results from the National Cancer Institute or National Toxicology Program study as questionable (104).

- Titanium dioxide was used as a control in a study on the acute cytotoxicity in 3T3 mouse fibroblasts (22).

- Titanium dioxide was not mutagenic in a bootstrap analysis of four *in vitro* short-term tests. The tests were: *Salmonella typhimurium* assay, mouse lymphoma L5178Y cell mutation assay, chromosomal aberration assay in CHO cells, and sister chromatid exchange test in CHO cells (7).

- Titanium dioxide did not induce sister chromatid exchange or chromosomal aberrations in Chinese hamster ovary cells with or without S9 activation (52).

- See Related References 148-151 for more information.

E. Developmental and Reproductive Toxicity

- No information is available.

F. Metabolism

- The deposition, retention, and clearance of TiO_2 particles in normal rats under varying conditions were determined. Assuming that the particle parameters are constant, the deposition can be predicted if the lung weight, concentration of TiO_2 in the air, and time of exposure are known. The clearance of particles was followed for up to 140 days. The retention half-time after exposure is 14 days for approximately the first eight days and 88 days thereafter. Experimental emphysema produced by aerosol inhalation and intratracheal injection of papain reduces the clearance rate of TiO_2 particles (29).

- By use of the nontoxic-particle-challenge system, the integrated alveolar clearance was measured in rats by serially sacrificing them after exposure to TiO_2 aerosol and determining the amount of TiO_2 retained in the lung. Prior to exposure to TiO_2, groups of animals were exposed to 0.1, 1, or 20 ppm of SO_2 for seven hours/day, five days/week for a total exposure of 70-170 hours. The results indicate that SO_2 affects the clearance of "inert" particles. The lowest exposures showed slight stimulation or no effect on clearance, whereas a depression of clearance was seen after 170 hours of exposure at 1 ppm. Short-term exposure at higher concentrations appear to be tolerated better than longer exposures at low concentration (30).

- A suspension of TiO_2, containing 2.5 g of TiO_2 per 100 mL of 5% aqueous dextrose was injected slowly into rat caudal veins. Ten randomly selected hepatic samples 24 hours after 500 mg TiO_2/kg injection gave values of 8.05 $\pm$ 0.27 mg/g of TiO_2. Removal of TiO_2 from blood occurred at an exponential rate. In the retroperitoneal space of a female rat, 25 lymph nodes were identified 24 hours after an injection of 37.5 mg TiO_2. Seven of

these nodes were intensely white and had a high TiO_2 concentration. These white celiacs (five to seven per rat) were in two clusters: one to three around the celiac axis in the epiploic foramen; two to five near the tail of the pancreas in the retroperitoneal space. Gross whiteness of lymph nodes containing 2 mg/g tissue was not accompanied by pathologic changes. In older rats, after partial splenectomy or hepatectomy before TiO_2 injection, the concentration of TiO_2 in liver was not changed compared with controls. However, the number of white celiacs and the concentration of TiO_2 in these nodes decreased after the partial hepatectomy. These white celiacs are the lymph nodes of the liver (50).

- Two strains of commonly used experimental rats were compared with regard to lung clearance of TiO_2. The Fischer 344 inbred rats retained fewer particles after a seven-hour exposure than the large outbred Long-Evans rats (31).

G. Biochemical Studies

- Acid phosphatase activity and cell morphology were followed using mouse peritoneal macrophages as a toxicity test model in vitro. The cells were given TiO_2 and five Ti pigments with different coating materials at 100 ug/mL of culture medium. The cell reactions were studied from one to 17 days. Ti particles inhibited the acid phosphatase activity of these cells compared to controls. In comparison to untreated cells, the activity of this enzyme increased in most groups studied, being highest in the control cells (2.0 to 3.5 times) after seven days. The Ti pigments did not cause the drastic alterations in these cells as seen with quartz and asbestos particles, but Ti pigments were not harmless to the mouse peritoneal macrophages with the dose and culture times used (88).

- An in vivo system, based on bronchopulmonary lavage, was used to compare a fibrogenic dust (quartz) and TiO_2, a reputedly inert material. The most obvious difference was the prolongation, with quartz, of an initial inflammatory response. The changes were assessed by cytological investigations and by biochemical analysis of recovered fluids, cells, and lung homogenates. There was evidence of a significant disparity between the cellular and biochemical data one day following instillation of quartz, which may be useful as an indicator of acute toxicity. The differences between the responses of alveolar macrophages after either quartz or TiO_2 instillation were not marked. However, polymorphonuclear leukocytes infiltrated the lung over an extended period after quartz instillation. Their subsequent lysis may indicate a role in the pathogenesis of pulmonary fibrosis (80).

- The effect of i.p. injection of a TiO_2 dust on splenic lymphocyte antibody-forming cells in immunized mice was studied. TiO_2 decreased the number of plaque-forming cells by about 33%. Systemic immunomodulation after local deposition of mineral dust may be important to the development of disease (109).

- Immunostimulatory effects of respirable mineral dust particles on alveolar macrophages (AM) and T lymphocytes were tested in vitro. When rat AM were incubated with non-fibrogenic TiO_2 particles, there was no significant interleukin 1 (IL-1) activity generated into the culture supernatants (89). There was also no interleukin 2 activity detected (90).

- Changes in the polymorphonuclear leukocytes (PMN) and alveolar macrophage (AM) populations from bronchoalveolar lavage fluid (BALF) seven days after instillation of TiO_2 was investigated. Results show that TiO_2 stimulates a slightly increased population of PMNs in the BALF compared to saline-dosed animals, and the majority of AMs contain TiO_2 particles (94).

- Substantial time-dependent fibrinolysis was noted in the mesothelial cells of female, syngeneic HAN-rats up to 24 hours after plating onto fibrin mats. Significant reductions in plasminogen-dependent fibrinolysis occurred at 1 ug/well with quartz and 3 ug/well with quartz and TiO_2. The findings suggest that both plasminogen-dependent and independent fibrinolysis are produced spontaneously by rat mesothelial cells in culture (20).

- Five naturally occurring and 11 synthetically produced TiO_2 specimens were studied for the ability of each to lyse erythrocytes and then compared with quartz. Only two synthetic rutiles were active. The H-bonding ability of the surfaces of these rutiles were compared with inert rutile and quartz; the binding properties of the active rutile were consistent with those properties associated with biologically active quartz. The biological activity of the polymorphs, as indicated by their hemolytic activity, depend on the surface properties of the crystals (86).

- The influence of crystal structure on lung inflammation and fibrosis was studied in vitro and in vivo. In vitro, human erythrocytes labeled with ^{51}Cr were incubated with anatase or rutile. The extent of hemolysis was determined by measuring leakage of ^{51}Cr into the medium. In vivo, mice were administered anatase or rutile by intratracheal injection. Six weeks later they were killed. In each experiment, the amount of each crystal used was chosen to provide identical surface areas. The % occupied volume of each crystal was calculated from data on the

unit cells. In vitro, rutile and anatase showed little hemolytic activity. In vivo, rutile and anatase caused no significant increases in wet lung weight, lavage protein content, or lung hydroxyproline concentration, and a minimal inflammatory or fibrotic response in the lungs (119).

- The ability of different TiO_2 samples to induce production of reactive oxygen metabolites by human polymorphonuclear leukocytes was studied. Pure rutile or anatase preparations show only a weak chemiluminescent response. Surface-modified TiO_2 causes a strong chemiluminescent response with a biphasic configuration resembling that of quartz. Coated TiO_2 exhibited a different mode of cell activation. The chemiluminescence-inducing activity of the different TiO_2 studied did not correlate with their hemolytic activity (49).

- Immunogold-silver staining was used to identify T lymphocytes, T lymphocyte subsets, and B lymphocytes in lung tissue from mice injected intratracheally with titanium dioxide. No lymphocyte response was observed in this tissue (58).

- See Related References 152-184 for more information.

H. Human Exposure

- A 22-year old man had an unusual pigmentary disease induced by TiO_2. The use of a topical cream containing TiO_2 caused a xanthoma-like appearance on the patient's penis. Electron probe microanalysis helped to establish the cause of the balanitis. The initial erosive herpetic lesions probably allowed increased percutaneous penetration of the TiO_2 (25).

- A farmer underwent lobectomy due to a lung tumor. Despite no clear evidence of previous occupational dust exposure, heavy deposits of birefringent particles and slight pulmonary fibrosis were found during histopathological examination. The major components of the dust were identified as mica, talc, and silica. Minor components included asbestos fibers and rutile fibers. Mica, quartz, feldspars, and rutile fibers were found in the soil from the farmer's potato storehouse (46).

- A 53-year old man was engaged in packing TiO_2 for about 13 years. At autopsy, a papillary adenocarcinoma was located in the right lung. Titanium was diffusely deposited in the lung and was engulfed by macrophages in the interstitium and alveolar spaces. Slight fibrosis of the interstitium around bronchioles and vessels was noticed as an effect of titanium deposition (121).

- A group of five adult human males ingested 5 g of TiO_2 daily for three days given in a milk suspension. No adverse effects were reported, and no significant increase in the amount of Ti in the urine was seen (2).

- No significant pulmonary alterations were reported among workmen employed in enclosed workshops with TiO_2 dust (116).

- Analysis by x-ray fluorescence spectrometry and emission spectroscopy of lung specimens from three workers employed in processing TiO_2 pigments for nine to ten years showed significantly higher Ti levels, compared to lung specimens from a general autopsy population. By light microscopy, Ti is birefringent and distinguishable from carbon. Deposits in the pulmonary interstitium were associated with cell destruction and slight fibrosis. TiO_2 was also found in the lymphatic system, although no reactive changes were seen in the lymph nodes. Electron microscopy showed TiO_2 particles within lysozymes of alveolar macrophages. These changes suggest that prolonged exposure to TiO_2 dust either alone or with other compounds such as Si, behaves as a mild irritant of the lung by an as yet unknown mechanism (26).

- A 49-year old man, exposed to TiO_2 dust for 15 years, showed extensive deposits of TiO_2 in both lungs corresponding completely to deposits of coal dust which were also present. The two different types of dust could be distinguished only by incident-light microscopy. The TiO_2 produced neither inflammatory nor fibrotic changes (64).

- Open lung biopsies and sputum specimens were obtained from three former workers of a TiO_2 pigment plant who were put on pension because of chronic bronchitis and partial pulmonary dysfunction. These studies showed that in the alveolar macrophages, lysosomes contained a significant amount of Ti as well as smaller amounts of Si, Al, Fe, and K (69).

- A radiological and clinical investigation was done among 136 workers in an ilmenite extracting plant in Ceylon. These workers were exposed to a number of minerals, of which the principal ones were ilmenite, rutile, and zircon. There was no significant difference in the incidence of radiological lesions of the chest between these workers and a control group drawn from the general population. Six workers had respiratory symptoms which first appeared after starting to work in the factory. These symptoms were non-specific in origin and due to the dust per se, and were unlikely to be due to exposure to the minerals (114).

- The disposition and accumulation of titanium pigment dust in the lungs of workers in TiO_2 plants were examined by electron microscopy, x-ray analysis, and atomic absorption spectroscopy. Microscopic examinations of lung samples showed large amounts of white, birefractive pigments, but no obvious fibrotic changes in the lungs were seen (91).

- There were pneumosclerotic changes in workers involved in the production of titanium white. The causative factors are SO_2, H_2SO_4 mist, and TiO_2 (71).

- Occupational exposure to TiO_2 for 18 years resulted in formation of reticular nodules, giving an infiltrative and encavated image in the central part of both lungs. Epitheloid follicles centered on crystal particles. Large amounts of TiO_2 were found in biopsy samples. Hypoxia was found and pneumoconiosis caused by TiO_2 (rutile) was diagnosed. Aspergillus fumigatus was found in exhaled air, and aspergillosis was treated with amphotericin while corticotherapy improved the radiology image, without improving the functional condition (3).

- Autopsy findings in a 55-year old man known to have been occupationally exposed to TiO_2 dust showed extensive pulmonary deposition of white pigment. The lungs did not show any inflammation or fibrotic changes (95).

- See Related References 185-193 for more information.

I. Epidemiology

- In a survey of 207 workers employed in the production of TiO_2 from ilmenite ore, clinically significant or symptomatic pulmonary disease was not frequently observed. Evidence of airways obstruction was found in 97 workers, including 79 who had never smoked regularly. This obstruction was not frequently accompanied by shortness of breath. Despite the fact that 90% of the workers were employed for 20 years or more, radiological changes consistent with pneumoconiosis were relatively few, and unrelated to the respiratory changes observed (19).

- A total of 2447 male employees with at least one-year employment before January 1, 1984 from two TiO_2 plants were studied; 1547 of them were exposed to TiO_2 and 900 were not. They were followed from 1956 through 1985 for cancer incidence and from 1935 through 1983 for mortality. In the TiO_2 cohort, eight lung cancer cases were identified as compared with 7.7 expected by the company rates. The observed number of lung cancer cases in the non-exposed cohort was eight as compared with 5.4 expected. There

were eight lung cancer deaths in the TiO_2-exposed cohort as compared with 17.1 expected based on U.S. rates; in the non-exposed cohort, there were 19 lung cancer deaths versus 19.9 expected based on U.S. rates.

The case-control analyses based on 16 lung cancer cases and 27 lung cancer deaths showed that the lung cancer risk was lower from TiO_2 exposure. The TiO_2 odds ratio was 0.6 for lung cancer incidence and 0.5 for lung cancer mortality, adjusting for age and other possible confounding chemical exposures (asbestos, titanium tetrachloride, and pigmentary potassium titanate).

Three TiO_2 exposure indices were used to evaluate the dose-response relationship: duration of exposure, cumulative exposure index, and time-weighted average exposure. No linear increasing trend was seen between any TiO_2 exposure index and lung cancer risk (incidence or death). The risk of having chronic respiratory disease was not elevated from TiO_2 exposure. There was no dose-response relationship between TiO_2 exposure and chronic respiratory disease.

503 active employees were evaluated for chest radiographic abnormalities. Of them, 355 were exposed to TiO_2 and 148 were not. No pulmonary fibrosis cases were found in either group. Nineteen (5.4%) cases of pleural thickening/plaques were identified in the TiO_2-exposed group and five (3.4%) in the non-exposed group. Two nodule cases were found in each group. There was no association between TiO_2 exposure and pleural thickening/plaques and nodules. No dose-response relationship was seen (13,14,24).

- A cross-sectional survey of 209 titanium metal production workers was done. Work in areas where there was exposure to titanium tetrachloride and titanium dioxide particulates was associated with reductions in ventilatory capacity. Pleural disease (plaques and diffuse thickening) was present in the chest radiographs of 17% of the subjects and was associated with the duration of work in titanium manufacturing. It was also associated with past asbestos exposure. After control for asbestos exposure, it remained associated with titanium manufacturing (39).

- Fifty-eight workers occupationally exposed to TiO_2 dusts underwent repeated laryngological and cytological examinations of their nasal mucous membrane smears. The clinical exam showed chronic rhinitis (77%) and pharyngitis (50%). The cytological test revealed metaplasia of the respiratory epithelium, toward squamous epithelium in all smears. The rate of catarrhal changes and the degree of epithelial metaplasia were found to vary with the duration of daily exposure. The changes in epithelium and nasal mucous membrane occurred after six months' exposure (75).

- In a June 1981 NIOSH study, 65 current and former workers at a kaolin mine and mill were examined by chest radiography, spirometry, and questionnaire. Five (13%) of 39 current workers and three (19%) of 16 former workers with $\geq$ five years' exposure had radiographic evidence of pneumoconiosis. Conglomerate upper lobe lesions were present in four of these eight workers. Current workers with < five years' exposure showed no evidence of pneumoconiosis. Lung function tests showed significant reductions in forced vital capacity, forced expiratory volume/second, and peak flow rate in kaolin workers compared with a control group. Airborne dust was composed of 96% kaolinite and 4% TiO_2 (103).

J. Aquatic/Environmental Studies

- 96-hour LC50 (sheepshead minnow) = < 370 > 240 ppm (24).
- 96-hour LC50 (opossum shrimp) = < 400 >300 ppm (24).
- The aquatic 96-hour TLm for rutile TiO_2 is > 1000 ppm (species not stated) (47).
- The toxicity of effluent from a TiO_2 factory containing H_2SO_4 residue with soluble metallic salts and insoluble material (i.e., silica) on fish, decapods, and mollusks was studied. The effluent caused changes in pH and oxygen depletion of the seawater. Sublethal effects of the ferrous salts were also studied. Dilutions of effluent less than 1:50 were 100% lethal concentrations for all organisms used, while a 1:200 dilution was a 50% lethal concentration for fish at 36 hours and for other organisms at 48 hours. Death of organisms at this concentration was caused by pH changes and oxygen depletion and did not account for the effect of the precipitants. Below this level, precipitation started soon after mixing with seawater causing the death of organisms by choking their gills and siphons. Dilutions $\leq$1:1000 were 96 hour 0% lethal concentrations (70).
- Toxic dilutions of a TiO_2 manufacture effluent were 1/2000 and 1/1000 for Asterionella japonica, approximately 1/2000 for Artemia salina, and approximately 1/4000 for Carassius auratus. Accumulation of titanium by some of the members of food chains examined were 2.1-3.9 ug/g in mollusks, 5-7 ug/g in crustaceans, $\leq$16 ug/g in Carassius auratus, and no accumulation by mice fed contaminated marine organisms for six months (5).

- Perch (Perca fluviatilis) and bleak (Alburnus alburnus) exposed for 14 and 28 days to TiO_2 industry effluents at 300, 400, or 600 uL/L (for perch) and 300, 500, or 1000 uL/L (for bleak) showed a decreased ability to compensate for torque in rotating current at the higher concentrations. The fish suffered from brown gill precipitate, but it was unknown if this led to the observed results (65).

- Thirty flounder were exposed to effluent from a TiO_2 manufacturing facility in southern Finland (daily discharge was approximately 10,000 m^3). The control group was kept in filtered brackish water. The low-dose group was exposed to 370 uL effluent/L of brackish water. The high-dose group was exposed to 685 uL effluent/L of brackish water. After two weeks exposure to the effluent, significant dose-dependent reductions of sodium and chlorine resulted. Blood plasma potassium concentrations did not change between exposure groups and controls. The osmolality differences are attributed to a brown precipitate found on the gill lamella consisting of an iron-titanium complex. The effluent-exposed flounder revealed increased levels of blood glucose and blood lactate, probably due to shock (59).

- See Related References 194-206 for more information.

K. Miscellaneous

- The Real-Time Simulation Air Quality Model (RAM) indicates that 90% of the SO_2 violations in the St. Louis, Missouri area were caused from plants manufacturing titanium oxide paint pigments by the sulfate process (102).

- An amount of powdered SiO_2 which by itself would not produce lung irritation will aggravate the effect of TiO_2. In general, the lesions are similar to those produced by the TiO_2 (78).

- The action of a dust, comprised of 54.7 parts TiO_2, 38.7 parts FeO, 2.16 parts SiO_2, 1.09 parts MgO, and 3.35 parts of other components, on the respiratory organs of rats was studied after 50 mg of the dust in 0.6 mL of saline was introduced into the trachea. Introduction of the Ti dust resulted in a diffuse proliferation process of the lymphoid tissue around the bronchi and only slight irritation of the lymph nodes. The irritating effect of this dust was stronger than that of pure TiO_2 (79).

- The effect of dust containing carbon, TiO_2, or SiO_2 on the pulmonary system was examined in rats. SiO_2 presence in dust caused an increase in the membrane passage and lymph drainage (72).

- Intratracheal administration of a mixture of 48 mg TiO_2 and 2 mg quartz induced, in rats, fibrosis as shown by the high hydroxyproline content of the lung. The degree of SiO_2-induced fibrosis was decreased by subcutaneous administration of poly(vinylpyridine N-oxide) (101).

- Inhalation of TiO_2 for 20 minutes, two or fours days before inhaling quartz, diminished pulmonary retention of the quartz. When the TiO_2 was given on the same day as quartz, it was ineffective (27,28).

- The ability of fine particle TiO_2 (MT-100) to prevent UVB-induced DNA damage in skin was evaluated in female hairless mice. At one hour after UVB irradiation, DNA synthesis was suppressed, but after 48 hours it was increased by five-fold over controls. Complete protection against this increased DNA synthesis was afforded by 1% MT-100 (107).

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April 11, 1990
PJL:pm:PJL1.8