INDUSTRIAL HYGIENE REPORT

OFM

DOWELL DIVISION

AN OPERATING UNIT OF THE DOW CHEMICAL COMPANY

DATE ISSUED: May 4, 1983

DEPARTMENT	ACCOUNT NO	PROGRAM NUMBER
INDUSTRIAL HYGIENE	70-10	IH5-0043-01

TITLE

PERSONNEL EXPOSURES TO ARSENIC DURING INDUSTRIAL CLEANING SERVICES VETROCOKE UNIT, AVON REFINERY, TOSCO CORPORATION, MARTINEZ, CALIFORNIA, APRIL 8-11, 1983

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DESCRIPTIVE SUMMARY WITH CONCLUSIONS

SUMMARY

An industrial hygiene survey was conducted while Dowell employees from Pittsburg and Torrance, California chemically cleaned a Vetrocoke system contaminated with arsenic. Personnel exposures to arsenic were acceptable when the recommended protective equipment was worn.

All personnel were informed about the consequences of exposure to arsenic, methods to reduce one's exposure from airborne arsenic as well as methods to protect individuals from surface contamiantion. Contingency plans were established for spills and leaks in an effort to minimize the potential hazard.

Dowell was contracted by IT Corporation to perform the chemical cleaning; IT was the primary contractor for the unit outage. The Industrial Hygiene department from IT worked with Dowell to ensure that all persons involved with the cleaning, Dowell, IT and other mechanical contractors, were adequately protected.

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PLAINTIFF'S EXHIBIT

DOW-2531

CONCLUSIONS

1. Personal protective equipment was required (slicker suit, Tyvek® coveralls) to reduce exposures to arsenic found on contaminated surfaces. Respirators were worn while a contractor crew demolished a cement pad adjacent to the C-4 tower, potentially contaminated with arsenic. No arsenic was detected in the air samples, analyzed after the demolition.

2. The use of V-675 helped reduce the chemical hazards of the job. The use of a conventional mineral acid, (i.e., HCl) could have formed arsenic trichloride or arsine gas both of which are undesirable.

3. Dowell employees reviewed the consequences of exposure to arsenic as well as V-675 before the job began. The protective equipment required to conduct the job was demonstrated.

4. Each Dowell employee was examined by a physician contracted by IT Corporation prior to the beginning of the cleaning. The examination met the requirements of OSHA Regulations 29CFR 1910.1018.

JOB DESIGN

The Vetrocoke system in the Avon Refinery contained three major components which were contaminated with an arsenic bearing scale.

Fin-fan coolers
CO_2 absorber (C-3)
Carbonate Regenerator (C-4)
and Associated Piping

V-675 was selected to dissolve the scale for several reasons including,

- avoid production of arsine gas when using a low pH solvent
- prevent plating of arsenic on cleaned surfaces
- avoid production of arsenic trichloride when using hydrochloric acid.

The system was filled with 50,000 gallons of diluted V-675 and circulated at 200°F. until the arsenic concentration in solution leveled off. The solvent was circulated and heated using the existing process pumps and steam. No Dowell pumping equipment was contaminated with arsenic.

The job required a supervisor and two operators for each shift (2 shifts per day). The job began Saturday, April 9, and lasted through Tuesday, April 12, 1983. Foam was generated near the end of the job and escaped from the vent hose laying on the ground near C-4 tower. The foam was contained in the containment area. Also, a leak occurred such that approximately 100 gallons of contaminated solvent was released from C-4. The spill stayed within the containment walls and was diverted to a holding tank for processing. Exposures to the solvent were minimized and no significant exposure occurred while responding to the spill.

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CONSEQUENCES OF EXPOSURE

Arsenic is a heavy metal which accumulates in the body and can result in gastrointestinal disturbances or skin disorders such as keratitis and pigmentation. Arsenic has also been indicated as a suspect carcinogen[1,2]; Epidemiology studies indicate an increase in skin and lung cancers for workers in the mining industry (i.e., copper smelting) and agriculture services (i.e., arsenic-bearing insecticides and sheep dipping). However, laboratory studies cannot duplicate the cancers in animals; it is suspected that cancers result from the synergistic effects of exposures to arsenic and other environmental exposures (i.e., smoking or acid gases). Arsenic may enter the body by either ingestion or inhalation such that both routes of exposure should be controlled.

The toxicity of the arsenic is dependant on its chemical form, primarily it's solubility in water. Selection of the chemical used to dissolve the arsenic scale is important; one should avoid forming arsine gas, a reaction product of strong acid and metals such as zinc or aluminum. Arsenic trichloride may be created when using hydrochloric acid as the solvent; arsenic trichloride is a severe irritant to the mucous membranes such as the eyes and nose. Skin contact may result in blistering; a lethal dose may be received by absorption of arsenic trichloride through the skin.

Chelated arsenic, such as formed when dissolved with V-675, is not readily accummulated in the body and skin absorption is reduced. The liver and kidney can excrete the arsenic more readily in the chelated form than in other chemical forms.

Exposures to arsenic should not exceed 10 micrograms per cubic meter (10 $\mu g/m^3$) when averaged over an 8 hour work shift[3,4]. Surfaces should be kept free of accumulations of arsenic by washing with water or good housekeeping procedures. Permissible levels of arsenic contamination have not been established. However, it is important to establish a background level before the job begins. Wipe testing surfaces during the job indicate problem areas before airborne arsenic concentrations become excessive.

1 "Patty's Industrial Hygiene and Toxicology - 3rd Revised Edition," Wiley-Interscience, New York, New York (1981) IIA page 1526-1528.

2 Occupational Exposure to Inorganic Arsenic. Washington D.C., National Institute for Occupational Safety and Health, (1975) Publication Number 75-149, page 28-56.

3 General Industry Safety Orders, State of California, Title 8, Section 5214 b, 5-30-81.

4 Occupational Safety and Health Administration, U.S. Department of Labor, 29 CFR 1910.1018c, 7-27-78.

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PROTECTIVE EQUIPMENT

Employees wore personal protective equipment when working inside the contaminated area. The protective equipment included:

Tyvek disposable coverall
Neoprene slicker suit
Rubber gloves
Goggles
Neoprene boots
Hard hat

The slicker suit was worn to protect from drips and sprays that were possible when the Vetrocoke system was filled and at operating temperature.

Respirators were required by mechanical contractors when the trays were removed from the towers (C-3 and C-4) prior to Dowell's chemical cleaning. Air samples collected by IT during this procedure indicated no detectable arsenic outside of the towers in the process area. Half-face respirators with high efficiency particulate filters manufactured by Scott were worn by Dowell employees when a potential airborne exposure existed while contractors broke up a cement pad nearby.

Only one entrance to the process area was available once the system was filled with water. This was required to restrict access by unauthorized persons. To leave the contaminated area, an employee proceeded to the decontamination trailer to remove the outer protective equipment (slicker suit and boots) leaving the Tyvek disposable suit. At the end of the shift, each employee showered and changed into street clothes in a separate locker room, designated as a non-contaminated area. The protective equipment (slicker suits and respirators) was cleaned by IT and available for the next shift. The Tyvek disposable suit was replaced at least at the end of each shift.

TRAINING

A training session was conducted before the job began to review operation procedures and Industrial Hygiene aspects of the job. Emergency procedures were discussed with specific shutdown procedures.

The Industrial Hygiene procedures necessary to reduce exposures were incorporated into the job design and demonstrated during this training session. These procedures included:

1. Consequences of exposure to arsenic.
2. Procedures to enter and leave process area.
3. Methods to remove contaminated clothing.
4. Selection and inspection of respirators.
5. Correct method to don respirator.

MEDICAL SURVEILLANCE

Each Dowell employee completed a medical physical prior to the job. The physician covered the following items:

- Comprehensive Medical History
- Posterior Chest X-ray
- Examination of the skin looking for lesions or keratosis
- Employee's ability to wear a respirator.

This examination was recommended by OSHA as adequate to discover problems an employee may encounter while working with arsenic. All data generated by the physician was transmitted to Dowell's Medical Director for further evaluation.

IH SAMPLING

Air samples were collected by Dowell and IT during all phases of the job.

The samples collected by IT were taken while the towers (C-3, C-4) were open to the atmosphere and prior to Dowell's chemical injection. No arsenic was found in the process area while the trays were removed from the towers. This task represented worst case of the entire operation and the most restrictive requirements for work inside the process area.

Wipe tests were collected to determine the extent of contamination both in the process area and outside of the barriers before the chemical cleaning job began. No removable arsenic was found on any sample (see Figure 1). A wipe test indicates the extent of cleanliness in a specific area. Airborne concentrations can increase if contaminated surfaces are disturbed, such as by walking across a dry, contaminated floor or opening a contaminated line. Wet surfaces help to reduce the airborne levels. A wipe test also confirms the movement of the arsenic from restricted to non-restricted areas. It is important to confirm that clean areas such as locker rooms and eating areas are free of arsenic contamination.

Air samples were collected to measure airborne arsenic concentrations while the V675 was injected into the system (see Figure 2). The area samples were representative of areas frequented by Dowell employees; the samples were collected at breathing zone height (approximately 6 feet). Air samples were also collected during the job when exposure conditions changed. The vent line from C-4 discharged near the entryway where an area sample was taken. No arsenic was detected in the sample. Another sample was collected when a contractor used a jackhammer to cut a concrete pad adjacent to the process area. The cement was potentially contaminated with arsenic, such that respirators were worn until the sample analyses were completed. No arsenic was detected in any of the air samples.

IH SAMPLING (Cont'd)

Wipe tests were collected after the spill from C-4 to determine the extent of the clean-up required (see Figure 3 for results). Process equipment was washed off and the water was collected in a holding tank. IT provided decontamination services for any person potentially contaminated with the solvent. Exposures were minimized because limited access to the process area and effective procedures used by IT and Dowell.

ANALYTICAL METHODS

All samples, air and surface, were collected on glass membrane filters. Each filter was dissolved in 100 mililiters Ammonium Biflouride solution; an aliquot was analyzed by the atomic absorption unit provided in Dowell's Mobile Laboratory which was on location for the duration of the job. Detection limit for arsenic was approximately 0.1 milligrams per sample.

ADDENDUM

INDUSTRIAL HYGIENE REPORT IH5-0043-01

PERSONNEL EXPOSURES TO ARSENIC DURING INDUSTRIAL CLEANING SERVICES VETROCOKE UNIT, AVON REFINERY, TOSCO CORPORATION, MARTINEZ, CALIFORNIA, APRIL 8-11, 1983

RECOMMENDATIONS

1. Each future chemical cleaning project involving heavy metals (i.e., arsenic), should be reviewed to ensure that major routes of exposure have been controlled, including surface contamination.

2. Any Dowell employee working with heavy metals should satisfactorily complete a medical physical where the physician documents any limitations that the employees might encounter upon the use of protective equipment such as a respirator [29 CFR 1018. N6(C)].

3. Process equipment potentially contaminated with arsenic, should be washed with water after each shift to reduce the amount of arsenic available for exposure.

4. Drips and spills should be collected at their source (i.e., drip pan under pump packings) before allowed to create an exposure hazard.

5. Temporary barriers should enclose the process equipment being cleaned. The restricted area should prevent unauthorized personnel from entering the area. The restricted area should be large enough to contain any drips or leaks that may occur while the solvent is circulated. Wind speed and direction may be a factor.

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May 4, 1983

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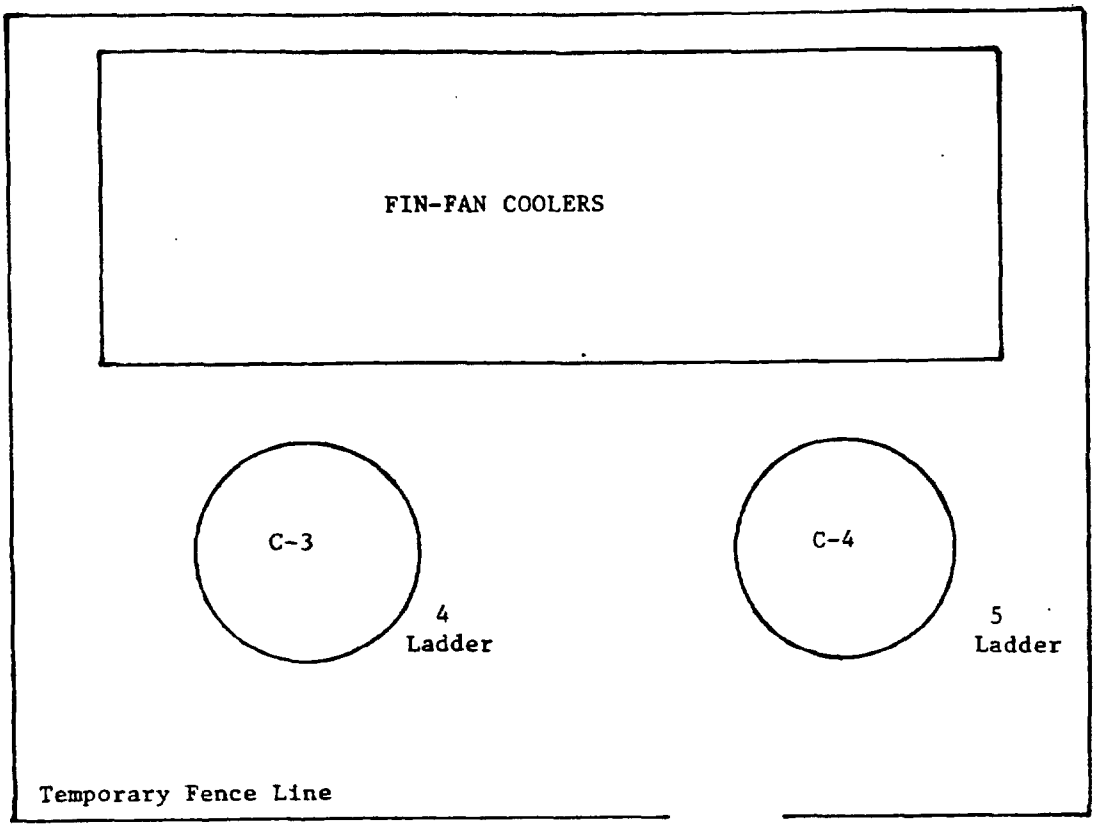
FIGURE 1

LOCATION OF WIPE TESTS TAKEN DURING REMOVAL OF TRAYS FROM C-3 AND C-4 BY PMC CONTRACTORS VETROCOKE PLANT, AVON REFINERY, APRIL 8, 1983



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- No detectable arsenic in any sample

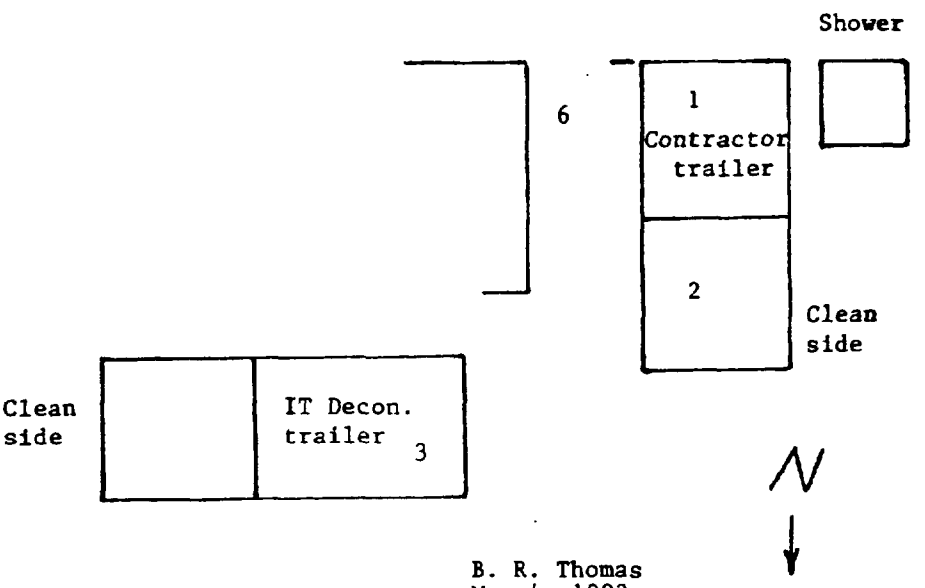

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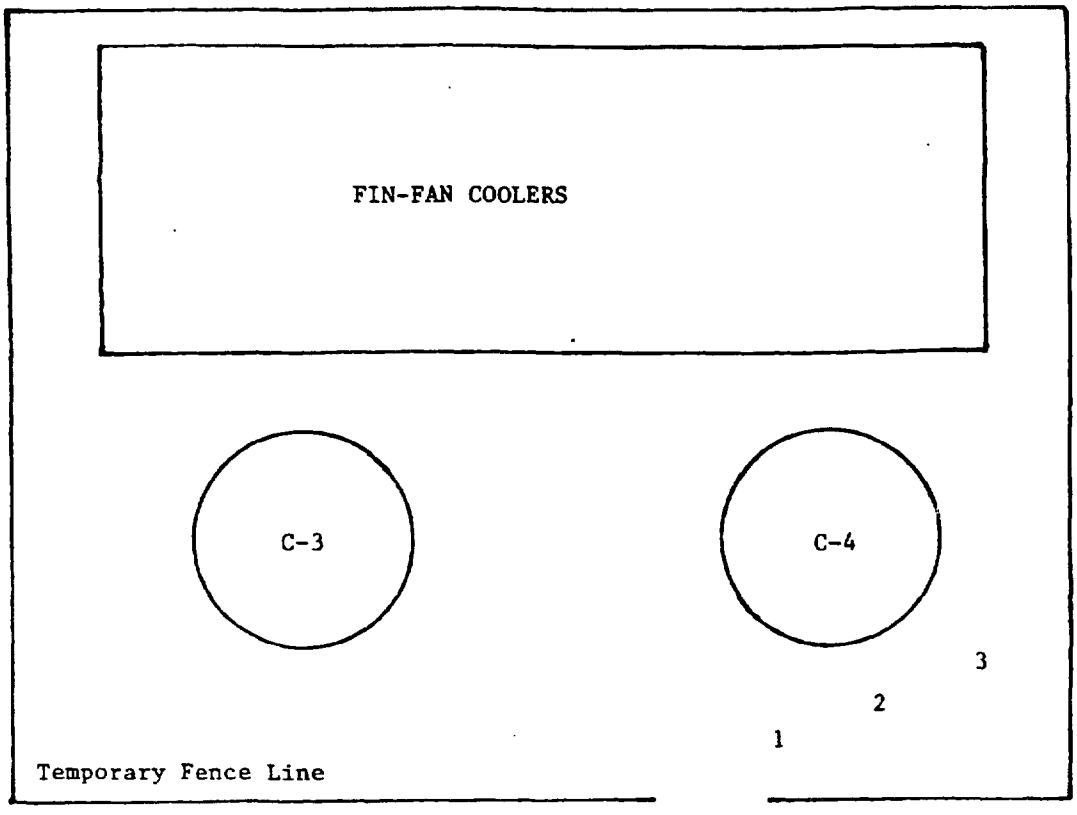
FIGURE 2

LOCATION OF AIR SAMPLES COLLECTED DURING CIRCULATION
OF V-675 VETROCOKE PLANT, AVON REFINERY, MARTINEZ, CA



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Sample #	Conditions	
1	System being filled	4/09/83
2	System at 200°F., near vent line	4/10/83
3	Cement pad being cut by jackhammer	4/11/83

Arsenic was not detected
in any air sample.

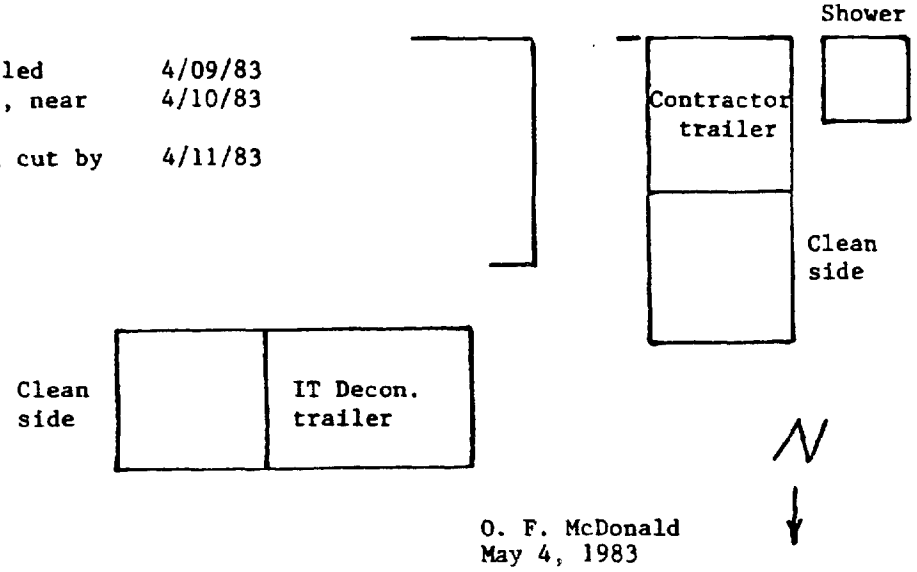

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FIGURE 3

LOCATION OF WIPE TESTS TAKEN AFTER EQUIPMENT WASHED DOWN
FOLLOWING THE LEAK, VETROCOKE PLANT, AVON REFINERY, MARTINEZ, CA
APRIL 11, 1983

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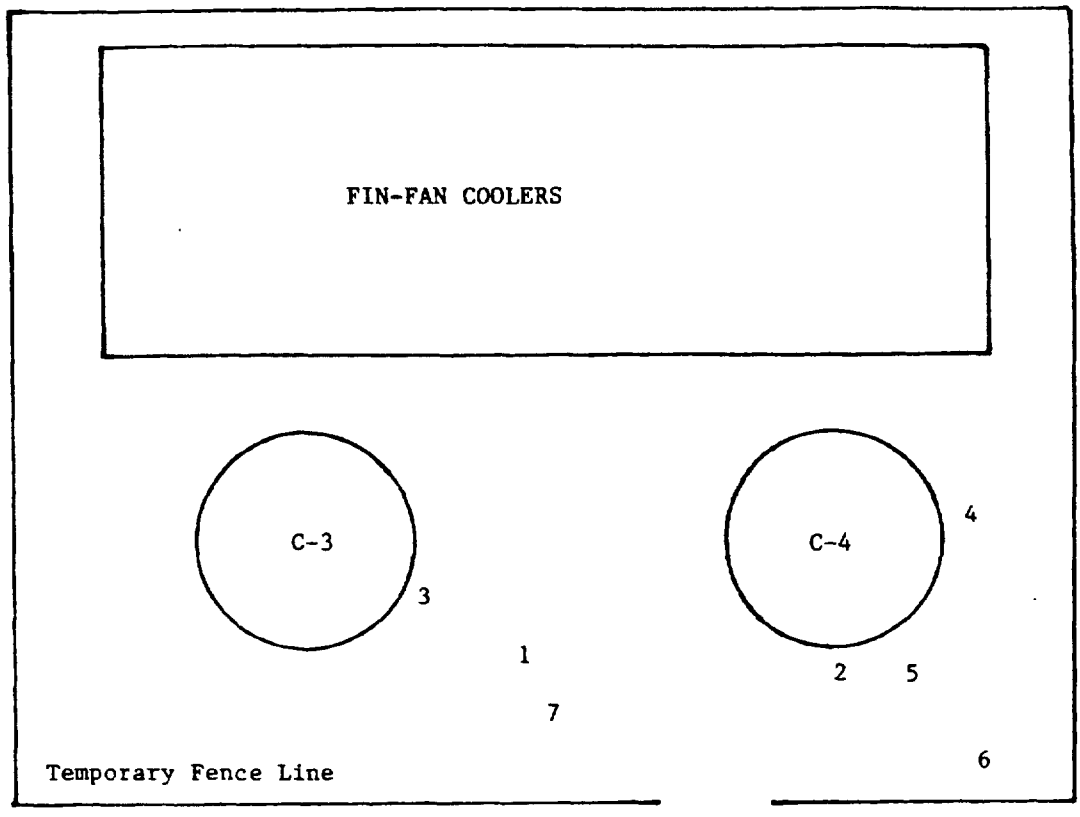

Sample #	Description	Results (mg/100cm^2)
1	Top of heat exchanger	ND
2	Ground level, immediately below spill	0.3
3	Side of tower C-3	0.1
4	Top of pipe adjacent to C-4	ND
5	Top of pipe adjacent to C-4	ND
6	Inside containment wall	0.2
7	Below heat exchanger	ND

ND - Not detectable

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ARSENIC and SOLUBLE COMPOUNDS

CAS: 7440-38-2

As

TLV-TWA, 0.2 mg/m³, as As

Arsenic, an element with atomic number 33, atomic weight 74.92, is in Group VA of the periodic table. The most common form of the element is a gray brittle crystalline solid with a specific gravity of 5.72, which sublimes at 613°C. It also exists in amorphous forms: black, specific gravity of 4.7 and yellow, specific gravity of 2.0, which is relatively volatile. Yellow arsenic is soluble in carbon disulfide; the other forms are insoluble in water or solvents, but dissolved by oxidizing acids.

Elemental or metallic arsenic is employed as an alloying agent for heavy metals, in special solders, and as a doping agent in silicon and germanium solid state products.

In addition to arsenic compounds discussed separately (As_2O_3, AsH_3 and lead arsenate, q.v.) many others find commercial application. The arsenites are important herbicides, calcium and other arsenates are insecticides; sulfides are pigments, rodenticides and used in pyrotechnics; gallium arsenide is in semiconductors; arsenic trichloride, a liquid with a boiling point of 130.5°C, is employed in chemical synthesis; the gaseous tri- and pentafluorides apparently have no important commercial uses. Many organic arsenic compounds, however, have been employed in medicine, or as war gases.

As with other metallic poisons, the toxicities, especially the acute toxicities, of arsenic compounds are related to their solubility in water. Thus, most arsenates and arsenites are acute poisons, while the sulfides are probably less toxic in an acute sense, but may be equally hazardous on prolonged exposure. Elemental arsenic is also less acutely toxic than its oxides, except for the rare yellow arsenic which is highly toxic, possibly similar to yellow phosphorus in some of its properties.

Systemic arsenic poisoning is rarely seen in industry, and still more rarely is it severe in character. According to Hardy,[1] it is hard to explain the difference between industrial and nonindustrial arsenic poisoning, but such variation is recorded in all industrialized countries. The usual effects on workers are local, on skin and mucous membranes, etc. A hoarse voice is characteristic of an arsenic worker, and a perforated nasal septum is a common result of prolonged inhalation of white arsenic dust or fume. A few documented cases of cirrhosis of the liver, however, due to occupational exposure to arsenic, have been recorded.[1]

Although the epidemiologic evidence is not complete, arsenic is considered by some to be a carcinogen, certainly of the skin, and perhaps of the bronchi.[2,3] Cancers from exposure to arsenic have followed: 1) the internal use of Fowler's Solution, an aromatic solution of potassium arsenite;[4] 2) inhalation and skin contact with sheep-dust, a mixture of sodium arsenite and sulfur;[5] 3) the combined inhalation of As_2O_3, SO_2 and other particulates from the smelting of ores containing arsenic (see documentation, arsenic trioxide production). Experimental cancers in animals have not been produced from As_2O_3 despite several attempts[6-8] and the conclusion of Vallee et al[8] was that "it is improbable that arsenic (per se) plays a significant role in the generation of cancer." The belief that other occupational factors are necessary for the development of cancer, in addition to arsenic exposure, has been expressed by others.[9]

A search of the world literature reveals no reports of industrial or experimental exposures solely to arsenic compounds which contain both environmental and toxicological criteria from which a TLV can be unequivocally based. Watrous and McCaughey[10] found concentrations of arsenic in a pharmaceutical plant averaging about 0.2 mg/m³, with no definite evidence of intoxication. Pinto and McGill studies a group of smelter employees and found an average urinary arsenic excretion of 0.8 mg/L.[11] The chief manifestation of toxic exposure was dermatitis, with perforation of the nasal septum, pharyngitis and conjunctivitis noted less frequently. A reasonable interpretation of the urinary arsenic levels would indicate an average exposure of about 0.2 mg/m³ of arsenic in air. Since individual concentrations as high as 4 mg/L of urine were found, it is probable that many workers were exposed at higher concentrations.

In its criteria document for inorganic arsenic, NIOSH in 1973[12] recommended 0.05 mg As/m³ (as a TWA) as a workplace air standard. This was changed in 1975 to 0.002 mg/m³ as a 15-minute ceiling.

The first limit was based primarily on reports of cancer among workers exposed to arsenic, as well as non-occupational cancer resulting from arsenic medications. The only pertinent environmental data cited not already noted consist of an average concentration of 0.56 mg/m³ computed from the paper by Perry et al[13] on an English sheep dip factory study, and a study by Lee and Fraumeni[14] in a smelting plant. Concentrations of 1.47, 1.56 and 1.50 mg/m³ were reported in "medium and high exposure areas" and 0.65, 0.17 and 0.002 mg/m³ in "light exposure areas." In both plants an increased incidence of cancer was reportedly found.

The Committee is not aware of any published explanation of the reasons for the reduction of the NIOSH 1973 recommendation of a TWA of 0.05 mg/m³ as a standard, to a ceiling of 0.002 mg/m³ in 1975.

Normal values of arsenic in urine, as recorded in the literature, vary from 0.013 to 0.046 mg/L,[1] to 0.13,[11] to 0.25.[15] The urinary excretion, in mg/liter, of elements that are freely eliminated by this route, such as fluorine, mercury and arsenic, is at most 2.5 to 5 times the occupational exposure in mg/cubic meter of air.[16] It is apparent that biological monitoring for arsenic by urinalysis would be of limited value in determining whether or not the NIOSH recommended standard was being met or exceeded.

It is possible that some arsenic compounds, the trichloride for example, might produce certain toxic effects at concentrations below 0.2 mg/m³ of arsenic. Data to substantiate this speculation are lacking. The contrary situation, that some compounds, or the metal itself, are chronically less toxic than As_2O_3, the form for which most information is available, seems more probable in the light of present knowledge. Therefore, a time-weighted average TLV of 0.2 mg As/m³ for soluble compounds of arsenic is recommended.

According to the 1980 compilation of occupational exposure limits of the International Labour Office,[17] the following countries had adopted the previous TLV of 0.5 mg/m³: Australia, Belgium, Finland, Japan, and Holland. Czechoslavakia, East Germany, Hungary and Poland specified the USSR MAC of 0.3 mg/m³; Romania and Switzerland, 0.2 mg/m³; Sweden 0.05 mg/m³; and Italy 0.25 mg/m³. Only three of 18 countries (West Germany, Italy and Sweden) designated arsenic and compounds as carcinogens, although Belgium and the Netherlands so characterized arsenic trioxide.

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ARSENIC TRIOXIDE PRODUCTION

CAS: 1327-53-3

As_2O_3

TLV-TWA, None
Appendix A2 — Suspected Human Carcinogen

The production of arsenic trioxide (As_2O_3) in the USA results from the smelting of copper sulfide ores of widely varying arsenic content. This process of smelting and refining presents a mixed exposure to arsenic, antimony and sulfur dioxide as well as to copper, cadmium, lead, selenium, silver, tellurium, thallium and mercury, the amount depending upon composition of the ore and the leaks in the furnaces and flues. The crude product contains 95% As_2O_3, from 10,000-20,000 ppm antimony, 300-600 ppm lead and iron, 100-800 ppm copper, 300 ppm zinc, and 15 ppm cadium and selenium, with more or less similar amounts of mercury and tellurium.

Two epidemiologic studies of copper smelting and refining have been reported by Pinto[1,2] in which the health effects from As_2O_3 exposure were statistically presented. In the first study (1953) the deleterious effects of As_2O_3 were principally irritation of exposed body surfaces, skin, conjunctivae and mucous membranes of the nose which in some cases resulted in perforation of the nasal septum. Of 835 urine determinations of 348 workers, arsenic values ranged from 0.1 to 6.44 mg/L, 95% of which were less than 2.1 mg/L, resulting in an average of 0.82 mg As/L urine, compared with 0.13 mg/L of 124 unexposed controls. No relation was found between urinary values and severity of the superficial lesions, and moderate cigarette smoking did not increase the amount of As in the urine.

The second study (1963) focused attention of the possible effects of As_2O_3 exposure on cardiovascular and cancer mortality during 1946 to 1960. Using the same measure of exposure, urinary As, as in the first study, Pinto and Bennett found no evidence that this degree of exposure produced a significant excess of systemic cancer or fatal cardiovascular disease in a total of 229 deaths in active plant employees and pensioners, which averaged 905 and 209, respectively. Pensioners consisted of males over 65 years with a minimum of 15-years exposure. Eighty percent of the cancer deaths occurred among heavy smokers, and 60% of the noncancer deaths were smokers. Relatively more cancer deaths occurred among the cohort control "nonexposed" (19.4% of all deaths) than among those exposed to As_2O_3 (15.8%). No concentrations of sulfur dioxide or other concurrent exposures were reported. Because urinary excretion values of the control cohort were higher than those reported by others,[3-5] relating the pulmonary cancer deaths to those from this cohort was felt[6] to lead to improper conclusions.

Indeed, a review of death certificates for the county in which the smelter was located, revealed 40 respiratory cancer deaths[7] instead of 18 reported by Pinto. Unfortunately the death certificates bore no information on what comprised the exposure or its magnitude, no information on length of employment of workers or where they worked in the operations, no information about previous employment or smoking habits.

In a restudy of mortality experience of 8047 smelter works, by Lee and Fraumeni,[8] which had been exposed during 1938 to 1964, and compared with the male mortality in the same states, a 3-fold over-all excess of respiratory cancer was found. This excess rose to 8-fold among the heaviest exposed smelters who had had 15 or more years of exposure. Although no arsenic, sulfur dioxide or silica levels were reported, respiratory cancer rates were positively correlated with estimated "high," "medium" and "low" levels of As_2O_3, and "high" and "moderate" levels of sulfur dioxide. An inverse correlation was found between observed-to-expected cancer deaths with "heavy," "medium" and "light" silica exposure groups, which was interpreted as "reflecting that work areas with heavy arsenic or heavy SO_2 exposure provided light silica exposure."

The importance of this study is that it may be the first to recognize that respiratory cancer in smelter workers may be promoted by concurrent exposures to respiratory irritants such as sulfur dioxide and silica, and "other metals" (not specified by the authors, but presumably antimony and lead).

In view of the fact that As_2O_3 by itself has never been shown to be a tumorigen in animals, despite several attempts,[9-11] it can only be concluded that if arsenic is to induce respiratory cancer in smelter workers, a promoter (or promoters) is a requisite. Consequently, arsenic trioxide production is given an A2 designation, a chemical substance associated with industrial processes, which are suspect of inducing cancer. No TLV is assigned at this time.

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MATERIAL SAFETY DATA SHEET

(Approved by U.S. Department of Labor "Essentially Similar to Form OSHA-20")

SECTION 1 — NAME OF PRODUCT

Chemical Name:	Catalog Number:
Arsenic	AX1735
Trade Name & Synonyms:	**Chemical Family:**
CA #7440-38-2	Metals
Formula:	**Formula Weight:**
As	74.92

SECTION 2 — PHYSICAL DATA

Boiling Point, 760 mm Hg (°C)		Specific Gravity (H_2O = 1)	5.73
Melting Point (°C)	sublimes > 615	Solubility in H_2O, % by wt. at 20°C	insoluble
Vapor Pressure at 20°C		Appearance and Odor	Silver gray crystals
Vapor Density (air = 1)		solid, lumps, powder	
Percent Volatiles by Volume		Evaporation Rate (Butyl Acetate = 1)	

SECTION 3 — FIRE AND EXPLOSION HAZARD DATA

Flash Point (test method) flammable	Flammable Limits	Lel	Uel

Extinguishing Media

Special Hazards and Procedures

Unusual Fire and Explosion Hazards: White fumes on sublimation, ignition

SECTION 4 — REACTIVITY DATA

Stable: X

Unstable:

Conditions to Avoid: Air and other oxidizers

Materials to Avoid

( ) Water ( ) Acids ( ) Bases ( ) Corrosives (X) Oxidizers

( ) Other (specify)

Hazardous Decomposition Products: Arsenic compounds

SECTION 5 — SPILL OR LEAK PROCEDURES AND DISPOSAL

Steps to be Taken in Case Material is Released or Spilled: Sweep up thoroughly. Place in closed container..

Waste Disposal Method: To be performed in compliance with all current local, state and federal regulations.

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SECTION 6 HEALTH HAZARD DATA

Threshold Limit Value

TXDS: mus-rat $_3$LDLo:25mg/Kg
0.5mg/m^3 in air

Effects of Overexposure Irritant to skin and mucous membrane.
Acute toxic effects develop ½ to 4 hrs. following ingestion: constriction of throat, vomiting, diarrhea, motor paralyses, death.

First Aid Procedures

Skin: wash with soap/water,get medical assistance.
Eyes: wash with water, get medical assistance.
Inhalation: remove to fresh air, get medical assistance.
Ingestion: get medical attention.

SECTION 7 SPECIAL PROTECTION INFORMATION

Ventilation, Respiratory Protection, Protective Clothing, Eye Protection

Work in well ventilated area. Wear protective clothes, gloves and face mask.

SECTION 8 SPECIAL HANDLING AND STORING PRECAUTIONS

Store in tightly closed container in a cool area.

SECTION 9 HAZARDOUS INGREDIENTS

(refer to section 3 through 8)

Arsenic

SECTION 10 OTHER INFORMATION

Workers continuously exposed to Arsenic should be subjected to periodic medical surveilance, urine and hair analysis.

EMERGENCY PHONE NUMBER (513) 631-0445

AUTHORIZED SIGNATURE _____

DATE ISSUED: _____

DATE REVISED: _____

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ST0408771

EM SCIENCE
111 Woodcrest Road, P.O. Box 5018, Cherry Hill, N.J. 08034-0395, Phone (609) 354-9200

MATERIAL SAFETY DATA SHEET

(Approved by U.S. Department of Labor "Essentially Similar to Form OSHA-20")

SECTION 1 — NAME & PRODUCT

Chemical Name:	Catalog Number:
Arsenic Pentoxide	AX1741
Trade Name & Synonyms: CA #1303-28-2	**Chemical Family:** Metal oxide
Formula: $3As_2O_5 \cdot 5H_2O$	**Formula Weight:** 779.6

SECTION 2 — PHYSICAL DATA

Boiling Point, 760 mm Hg (°C)		Specific Gravity (H_2O = 1)	4.09
Melting Point (°C)	315	Solubility in H_2O, % by wt. at 20°C	soluble
Vapor Pressure at 20°C		Appearance and Odor	White amorphous solid
Vapor Density (air = 1)			
Percent Volatiles by Volume		Evaporation Rate (Butyl Acetate = 1)	

SECTION 3 — FIRE AND EXPLOSION HAZARD DATA

Flash Point (test method) flammable	Flammable Limits	Lel	Uel

Extinguishing Media

Special Hazards and Procedures

Unusual Fire and Explosion Hazards

SECTION 4 — REACTIVITY DATA

Stable	Conditions to Avoid Exposure to air and oxidizers
Unstable X	

Materials to Avoid

( ) Water ( ) Acids ( ) Bases ( ) Corrosives (X) Oxidizers

( ) Other (specify)

Hazardous Decomposition Products Arsenic fumes

SECTION 5 — SPILL OR LEAK PROCEDURES AND DISPOSAL

Steps to be Taken in Case Material is Released or Spilled Sweep up and place in closed container.

Waste Disposal Method To be performed in compliance with all current local, state and federal regulations.

ST0408772

SECTION 6 — HEALTH HAZARD DATA

Threshold Limit Value

TXDS: oral-rat LD50: 8mg/Kg
0.5mg/m^3 as As

Effects of Overexposure Irritant to skin and mucous membrane.
Acute toxic effects develop ½ to 4 hrs. following ingestion.
Constriction of throat, vomiting, diarrhea, motor paralysis, death.

First Aid Procedures

Skin: wash with soap/water, get medical assistance.
Eyes: wash with water, get medical assistance.
Inhalation: remove to fresh air, get medical assistance.
Ingestion: get medical attention.

SECTION 7 — SPECIAL PROTECTION INFORMATION

Ventilation, Respiratory Protection, Protective Clothing, Eye Protection

Work in well ventilated area. Wear protective clothes, gloves and face mask.

SECTION 8 — SPECIAL HANDLING AND STORING PRECAUTIONS

Store in tightly closed container in a cool place.

SECTION 9 — HAZARDOUS INGREDIENTS

(refer to section 3 through 8)

Arsenic

SECTION 10 — OTHER INFORMATION

Workers continuously exposed to Arsenic must be subjected to periodic medical surveilance, urine and hair analysis.

EMERGENCY PHONE NUMBER (513) 631-0445

AUTHORIZED SIGNATURE _____

DATE ISSUED: 1/1/..

DATE REVISED: _____

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EM SCIENCE
111 Woodcrest Road, P.O. Box 5018, Cherry Hill, N.J. 08034-0395, Phone (609) 354-9200

MATERIAL SAFETY DATA SHEET

(Approved by U.S. Department of Labor "Essentially Similar to Form OSHA-20")

SECTION 1 — NAME & PRODUCT

Chemical Name:	Catalog Number:
Arsenic Trichloride	AX1742
Trade Name & Synonyms: Arsenic Chloride, Arsenious Chloride, Fuming Liquid Arsenic	**Chemical Family:** metal oxide
Formula: $AsCl_3$	CA #7784-34-1 — **Formula Weight:** 181.28

SECTION 2 — PHYSICAL DATA

Boiling Point, 760 mm Hg (°C)	130.5	Specific Gravity (H_2O = 1)	2.16
Melting Point (°C)	-18	Solubility in H_2O, % by wt. at 20°C	dec.
Vapor Pressure at 20°C		Appearance and Odor	oily liquid
Vapor Density (air = 1)			
Percent Volatiles by Volume		Evaporation Rate (Butyl Acetate = 1)	

SECTION 3 — FIRE AND EXPLOSION HAZARD DATA

Flash Point (test method) nonflammable	Flammable Limits	Lel	Uel
Extinguishing Media			
Special Hazards and Procedures	Extremely hazardous		
Unusual Fire and Explosion Hazards	Fumes on exposure to air		

SECTION 4 — REACTIVITY DATA

Stable	Conditions to Avoid: Exposure to air and other oxidants.
Unstable X	

Materials to Avoid

( ) Water ( ) Acids ( ) Bases ( ) Corrosives (X) Oxidizers

( ) Other (specify)

Hazardous Decomposition Products: Fumes of Arsenic compounds

SECTION 5 — SPILL OR LEAK PROCEDURES AND DISPOSAL

Steps to be Taken in Case Material is Released or Spilled	Dilute with water. Add dilute alkali and place into closed container.
Waste Disposal Method	To be performed in compliance with all current local, state and federal regulations.

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SECTION 6 HEALTH HAZARD DATA

Threshold Limit Value
TXDS: ihl-mus LCLo: 2500mg/m^3/10M
ihl-cat LCLo: 100mg/m^3/1H

Effects of Overexposure: Strong irritant (vesicant) to skin and respiratory tract.

First Aid Procedures
Skin: wash with soap/water, get medical assistance.
Eyes: wash with water, get medical assistance.
Inhalation: remove to fresh air, get medical assistance.
Ingestion: get medical attention.

SECTION 7 SPECIAL PROTECTION INFORMATION

Ventilation, Respiratory Protection, Protective Clothing, Eye Protection

Work in well ventilated area. Wear protective clothes, gloves, and gas mask with air supply.

SECTION 8 SPECIAL HANDLING AND STORING PRECAUTIONS

Extremely hazardous liquid. Store in tightly closed container in a cool place.

SECTION 9 HAZARDOUS INGREDIENTS

(refer to section 3 through 8)

Aresenic Trichloride

SECTION 10 OTHER INFORMATION

Workers continuously exposed to Arsenic compound must be subjected to continual medical surveilance, urine and hair analysis.

EMERGENCY PHONE NUMBER (513) 631-0445

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DATE ISSUED: 1/82

DATE REVISED: _____

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EM SCIENCE
111 Woodcrest Road, P.O. Box 5018, Cherry Hill, N.J. 08034-0395, Phone (609) 354-9200

MATERIAL SAFETY DATA SHEET

(Approved by U.S. Department of Labor "Essentially Similar to Form OSHA-20")

SECTION 1 — NAME OF PRODUCT

Chemical Name:	Catalog Number:
Arensic Trioxide	AX1744, 1745, 1747, 1750 120
Trade Name & Synonyms: Arsenious Oxide	Chemical Family:
Arsenous Acid CA #1327-53-3	metal oxides
Formula: As_2O_3	Formula Weight: 197.84

SECTION 2 — PHYSICAL DATA

Boiling Point, 760 mm Hg (°C)		Specific Gravity (H_2O = 1)	3.87
Melting Point (°C)	sublimes > 193	Solubility in H_2O, % by wt. at 20°C	slight
Vapor Pressure at 20°C		Appearance and Odor	White odorless powder
Vapor Density (air = 1)			
Percent Volatiles by Volume		Evaporation Rate (Butyl Acetate = 1)	

SECTION 3 — FIRE AND EXPLOSION HAZARD DATA

Flash Point (test method) nonflammable	Flammable Limits	Lel	Uel

Extinguishing Media

Special Hazards and Procedures

Unusual Fire and Explosion Hazards: White fumes on sublimation.

SECTION 4 — REACTIVITY DATA

Stable X	Conditions to Avoid
Unstable	

Materials to Avoid

( ) Water ( ) Acids ( ) Bases ( ) Corrosives ( ) Oxidizers

( ) Other (specify)

Hazardous Decomposition Products: Arsenic compounds

SECTION 5 — SPILL OR LEAK PROCEDURES AND DISPOSAL

Steps to be Taken in Case Material is Released or Spilled: Sweep up thoroughly. Place in closed container.

Waste Disposal Method: To be performed in compliance with all current local, state and federal regulations.

SECTION 6 HEALTH HAZARD DATA

Threshold Limit Value N/A

TXDS: orl-man LD50: 1430 ug/Kg
ihl-man TCLo: 700 ug/m^3/ih

Effects of Overexposure Irritant to mucous membrane.
Acute toxic effects develop ½ to 4 hrs. following ingestion.
Constriction of throat, vomiting, diarrhea, motor paralysis, death.

First Aid Procedures

Skin: wash with soap/water, get medical assistance.
Eyes: wash with water, get medical assistance.
Inhalation: remove to fresh air, get medical assistance.
Ingestion: get medical attention.

SECTION 7 SPECIAL PROTECTION INFORMATION

Ventilation, Respiratory Protection, Protective Clothing, Eye Protection

Work in well ventilated area. Wear protective clothes, gloves, and face mask.

SECTION 8 SPECIAL HANDLING AND STORING PRECAUTIONS

Store in tightly closed containers in a cool area.

SECTION 9 HAZARDOUS INGREDIENTS

(refer to section 3 through 8)

Arsenic compounds

SECTION 10 OTHER INFORMATION

Workers continuously exposed to Arsenic should be subjected to periodic medical surveilance, urine and hair analysis.

EMERGENCY PHONE NUMBER (513) 631-0445

AUTHORIZED SIGNATURE _____

DATE ISSUED: _____

DATE REVISED: _____

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3 ARSENIC, As

3.1 Source (57) and Production (1)

Arsenic is a ubiquitous element, being widely distributed in the earth in an abundance of about 5 g/metric ton in more than 150 As-bearing minerals, of which the most common are arsenopyrite ($FeAs_2 \cdot FeS_2$), enargite ($3\ Cu_2S \cdot As_2S_5$), realgar (AsS), and orpiment (As_2S_3).

Domestic production of white arsenic, arsenic trioxide (As_2O_3), however, is solely as a by-product of base-metal ores, chiefly copper ore (As content from a trace to 2 to 3 percent) and is from a single plant which does not release production figures. U.S. imports in 1973 amounted to about 11,500 short tons of As_2O_3, about 650 short tons of metallic As, and 263 short tons of sodium arsenate. Major foreign countries producing As_2O_3 include Mexico, Sweden, France, and the Soviet Union. Swedish gold ores contain 7 to 11 percent As.

Arsenic is usually marketed as the trioxide which is recovered as a by-product from

smelting copper-, lead-, and gold-bearing ores. Because As_2O_3 is readily volatilized during smelting, it concentrates in the crude flue dust which may contain up to 30 percent As_2O_3, the balance being oxides of Cu, Pb, Sb, and Zn. Crude flue dust is further refined by adding small amounts of pyrite which prevents formation of arsenites during roasting. After passing through cooling chambers As_2O_3 vapors of 90 to 95 percent purity are condensed. For a product of higher purity, the impure oxide is resublimed with a purity of 99 to 99.9 percent. Grades for marketing are white soluble (99 percent min. As_2O_3) and white insoluble, or crude (95 percent min. As_2O_3). Table 29.3.1 gives the composition of these two As_2O_3 products in terms of major trace element content (100). It is seen that even the refined As_2O_3 contains from 25,000 to 5000 ppm (2.5 to 0.5 percent) Sb_2O_3, but trace element content varies widely over the years, as noted in a crude sample from Asarco analyzed in 1956 (107) compared with data supplied in 1977 (100).

Metallic As can be prepared from mispickel ($FeS_2 + FeAs_2$) by heat decomposition and distilling the As condensed on the cooler surfaces of the retort. It can also be obtained by reducing As_2O_3 with Zr Commercial, 99+ percent. Arsenic contains 0.23 to 0.7 percent Sb, <0.001 percent Pb and Bi, 0.0005 to 0.0024 percent Fe, and <0.0001 to 0.0002 percent Cu (100).

Arsine, AsH_3, is produced whenever nascent H is liberated in a solution containing inorganic As, such as when metals containing As are subjected to reducing acids or pickling.

3.2 Uses (100) and Industrial Exposures

As_2O_3 is used in lead-base alloys for hardening lead used in battery grids, bearings, and cable sheathing, as a rust inhibitor in antifreeze, as an oxidizing and refining agent in glass manufacture, as a preservative in tanning and taxidermy, and as an ingredient in wood preserving. Arsenic compounds are widely used as a desiccant to facilitate stripper-harvesting of cotton. Sodium arsenite is used as a weed killer and in debarking of trees for wood pulp. Arsenic is used in shot-forming, changing the surface tension of lead and permitting the formation of perfectly spherical shot, in solder and steel as an alloying ingredient, in the making of sheep dip, and as an ingredient in growth and health promoters for swine and poultry. As_2O_3 is the starting product for pharmaceuticals such as arsenilic acid and cacodylates, and arsenates of calcium, copper, and lead are widely used as insecticides (see Table 29.3.2) and thus present serious exposure during application and in mixing, screening, drying, bagging, and drum-filling operations.

Forest workers applying silvicides of cacodylic acid and sodium methane arsenate represent a modern group exposed to potentially hazardous levels of organic arsenicals, unless strict precautions are taken (101).

Many potentially serious exposures to As occur in the smelting of arsenical ores. Highest exposures occur in the cleaning of flues and dust collectors, in loading and transporting the As_2O_3, and in repairing and cleaning furnaces. Uncontrolled stack effluents contaminate the soil and vegetation for miles around a smelter and have led to

Table 29.3.1. Composition of Refined and Crude As_2O_3

Component	Refined (100) (%)	Crude (%)
As_2O_3	98.5–99	96–98.5 (100)
Sb_2O_3	0.5–2.5	1.2 (107)[a]
Pb	0.03–0.25	0.05
Hb	0.015–0.55	0.002
Fe	0.1–0.2	0.06
Si		0.06
Al		0.05
Zn		0.02
S		0.02
Tl		0.02
Ca		0.01
F		0.01
Cl		0 005
Se		0.001
Te		Nil

[a] Arsenic spectrographically analyzed on a crude Asarco sample.

a variety of skin and mucous membrane lesions among members of an adjoining mining community (102).

Metallic As is finding new, but limited, use as a component of semiconductors in which its purity must exceed 99.999%. Calcium and indium arsenides have thus far found the greatest use. Metallic As is essentially nontoxic, and thus presents no exposure hazards; because the intermetallic arsenides are used in such small quantities and their toxicity is so low owing to their physiological stability (103), no adverse health effects from their production and use have been reported.

AsH_3 has no industrial uses except in certain analytic methods for As, but offers many potential exosures. Any operation in which reducing acids act on metals, or other substances containing As, is a potential source of the gas. Arsenides of electropositive metals yield AsH_3 with acids or even water, as do Pb–As alloys. Some strains of bacteria and fungi are capable of synthesizing AsH_3 on an As-containing medium.

3.3 Physical and Chemical Properties (104)

The physical and chemical properties of As and some of its industrially important compounds are given in Table 29.3.2.

3.4 Analytic Determination

The presently recommended method for sampling and analysis of As in air and urine is given in detail in the new NIOSH criteria document on inorganic As (105). In essence,

Table 29.3.2. Physical and Chemical Properties of As and Some of its Compounds (104)

Form of As	At. or Mol. Wt.	Sp. Gr.	M.P. (°C)	B.P. (°C)	Solubility
Arsenic (As)	74.92	5.73 (14°C)	817 (28 atm)	613 subl.	Insol. cold and hot water; sol. HNO_3
Arsenic trioxide (As_2O_3)	197.84	3.865 (25°C)	193 subl.	—	Sol. cold H_2O, 1.2 g/100 g; sol. hot H_2O, 11.46 g/100 g (100°C); sol. alcohol, alkalies, HCl
Arsine (AsH_3)	77.95	2.695 gas 1.689 liq. (84.9°C)	−116.3	−55	Sol. cold H_2O, 20 ml/100 g (20°C); sol. $CHCl_3$, C_6H_6
Arsenic trichloride ($AsCl_3$)	181.28	2.163 (14°C) liq. 6.25 vap	−18	130.2	Dec. cold, hot H_2O; sol. HBr, HCl, $PbCl_2$, alcohol ether
Arsenic pentoxide (As_2O_5)	229.84	4.32	Dec. 315	—	Sol. cold H_2O 150 g/100 g (16°C); 76.7 hot H_2O (100°C); sol. alcohol, acid, alkalies
Calcium arsenate (ortho) [$Ca_3(AsO_4)_2$]	398.07	3.620	—	—	Sol. cold H_2O, 0.013 g/100 g (25°C)
Copper acetoarsenite [$3Cu(AsO_2)_2 \cdot Cu(COOCH_3)_2$]	1013.7	—	—	—	Insol. cold H_2O; sol. acid, NH_4OH
Lead arsenate (diortho) ($PbHAsO_4$)	347.14	5.79	Dec. 720	$-H_2O$, 220	Insol. cold H_2O; sl. sol. hot H_2O; sol. HNO_3, caustic alkalies
Sodium arsenite (meta) ($NaAsO_2$)	129.91	1.87	—	—	V. sol. cold and hot H_2O; sl. sol. alcohol

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air samples are collected in the breathing zone of the worker on a cellulose membrane filter at a flow rate of 2 liter/min. For analysis, samples are ashed with a mixture of nitric, perchloric, and sulfuric acids, transferred to an arsine generator by the addition of either metallic Zn or sodium borohydride, and the arsine passed through the burner of an atomic absorption spectrophotometer. This recommended method exceeds past methods, the molybdenum blue, Gutzeit, and Marsh tests, in both precision and sensitivity.

3.5 Physiological Responses

Arsenic compounds can be absorbed into the body from industrial exposures chiefly by inhalation and ingestion. About four-fifths of the absorbed arsenic is widely distributed in the tissues including the liver, abdominal viscera, bone, skin, and particularly hair and nails, where it can be detected, many months after it has disappeared from the urine and feces, over and above that found normally from dietary sources. A very small amount is exhaled in the breath as trimethylarsine (106). It is important to note that industrial As exposures are to the trivalent form, which is considered to be somewhat more toxic than the pentavalent form.

3.5.1 Acute Toxicity

The reported acute toxicity for laboratory animals of As_2O_3 over the years has varied from 8 to 500 mg/kg body weight (107). Both crude and pure As_2O_3 in aqueous solution were found to be almost tenfold more toxic than As_2O_3 administered dry by the same route (rat LD_{50}, crude and pure, 23.6 and 15.1 mg/kg in solution vs. 214 and 145.2 mg/kg for the dry). As_2O_3 crude and pure in solution was more toxic for the rat of about the same relative age than for the mouse (rat LD_{50}, crude and pure, 23.6 and 15.1 mg/kg vs. mouse LD_{50}, 42.9 and 39.4 mg/kg). From these LD_{50}s it seemed that the crude was slightly less toxic than the pure for the mouse, considerably more toxic for the young than the old mouse (LD_{50}, pure, 39.4 vs. 47.6 mg/kg). No difference in acute toxicity was found between males and females of the species. There were, however, considerable differences in the toxicity among different strains of mice, almost twofold between Swiss Webster and C_3H strains (47.6 vs. 25.8 mg/kg). Marked hemorrhage of the stomach and intestines was reported in these studies (106). Fatty degeneration of the liver with cell necrosis and reparative changes following acute administration has also been reported (108).

No reports have been found showing that metallic As has appreciable toxicity, certainly not acute toxicity.

Acute As poisoning in human beings by ingestion is usually homicidal, suicidal, or accidental. The smallest recorded fatal dose is about 130 mg, but recovery has occurred after much larger doses. Death after a fatal dose averages between 12 and 48 hr. Symptoms of fatal poisoning are abdominal pain and vomiting, usually within an hour of ingestion, due to inflammatory changes in the mucous membranes of the stomach and

upper gastrointestinal tract. In some cases exfoliative dermatitis and peripheral neuritis follow recovery from the acute symptoms.

3.5.2 Industrial Exposures and Chronic Toxicity

Chronic signs of toxicity in workers exposed to As compounds are related chiefly to the skin, mucous membranes, gastrointestinal and nervous systems, and far less commonly to disorders of the circulatory system and the liver. The question of the carcinogenic action of As compounds, long debated for all As compounds generally, now would appear to be resolved at least for industrial exposures to As_2O_3. As_2O_3 is not carcinogenic per se, but requires a promoter, such as appreciable exposure to respiratory irritants such as SO_2, metal oxide fumes, or smoking, to elicit the carcinogenic response.

Dermal Effects. Dermal lesions have been by far the most common form of industrial poisoning by As compounds. Cutaneous lesions can result during the manufacture of insecticides involving As_2O_3 and copper acetoarsenite (109) or during production of As_2O_3 in copper ore smelting (110). Although acute dermatitis is more common than chronic, which may appear only after years of employment, the dermatitis starts with an erythema, associated with burning and itching, giving the skin a mottled appearance. If the dermatitis is on the face, swelling may occur, which either may disappear or may be followed by papular or vesicular eruptions. In addition to the face, the neck, forearms, wrists, and hands may be involved.

A prominent feature of chronic industrial skin lesions in the past is hyperkeratosis, often accompanied by hyperhidrosis (excessive sweating) especially of the palms and soles. Hyperkeratosis is characterized by cracking skin, thickening and drying of the skin, and warts (111), but a diffuse, "brawny" desquamation of the skin of the trunk and extremities with deeply pigmented areas has also been described and likened to Addison's disease (112). With modern exposure control methods, only one case of hyperkeratosis of hands and feet has been found in the last 30 years (113).

Arsenical melanosis is another common sign of overexposure to arsenicals. In a summary article (114) it was concluded that the melanin pigment contained no As but did contain lipids and melanin derived from As-altered cell metabolism, and that these arose chiefly in the corium and in lesser amounts in the epidermis.

Mucous Membrane Effects. Dermatitis of the face and eyelids is sometimes accompanied by conjunctivitis, with redness, swelling, and pain. Exposure to calcium arsenate insecticide resulted in corneal anesthesia and ulcer. Often there is irritation of the nose and pharynx, causing acute or chronic rhinitis, and of the bronchial passages.

Perforation of the nasal septum has occurred among copper smelter workers (115). Perforation is preceded by epistasis, irritation of the nose, and crust formation with obstruction to nasal breathing and necrosis of the septum. Arsenic dust coming in contact with the moist nasal membranes forms arsenious acid, which corrodes the septal mucosa.

Gastrointestinal Disturbances. True gastroenteritis is not common among industrial workers exposed to As compounds, but can occur. Pinto and McGill (115) found only one case among several hundred As_2O_3 production workers; however, digestive disturbances such as nausea and vomiting are occasionally reported. These signs are accompanied by others characteristic of arsenical poisoning as described above.

Peripheral Neuritis. Symptoms accompanying arsenical neuritis are pain and burning tenderness in the affected limbs and difficulty in walking, associated with arsenate sprays and dusts (111). In most cases, onset is gradual, with sensory disturbances in the extremities, numbness, and tingling sensations followed by severe weakness in both legs and feet.

Difficulty in differential diagnosis of arsenical neuritis from exposure to lead arsenate insecticide spray can be resolved by the findings of initial gastrointestinal disorders and the presence of Mees' bands in the nails, even without the presence of hyperkeratosis and numbness in the hands and feet. (Mees' bands are white striae in the fingernails.)

Although spot environmental and biologic analyses were made in some of the reports in conjunction with the various forms of As toxicity just summarized (111, 115), it was concluded (115) that spot air levels are of value only to engineers as a measure of the effectiveness of exposure controls. They are of limited value in predicting the frequency of dermal or systemic disease; with urinary As values commonly 4 to 5 mg/liter, only one doubtful case of systemic disease could be correlated with such levels.

Hematologic Aspects. A feature not commonly associated with As poisoning is hematologic changes. Six cases believed to be unequivocally diagnosed as systemic poisoning from inorganic As ingestion, and with characteristic symptoms such as nausea, fatigue, diarrhea, and pigmentation, 4 showed anemia and leukopenia in all six, thrombocytopenia in three. Disturbed erythropoiesis in bone marrow cells was found in three, and depressed or disturbed myelopoiesis in four. All hematologic changes disappeared in 2 to 3 weeks after cessation of As ingestion (116).

Metabolism, Mode of Action, and Therapy. Following absorption into the blood, arsenicals are distributed rapidly and widely to all tissues of the body. At 20 hr after radio-labeled sodium arsenite had been intravenously injected into a male cancer patient, the liver had the highest ^{76}As content of all tissues analyzed on a $m\mu c/g$ basis (117). Using liver as 100 percent, the kidney had 65 percent; the spleen, heart, jejunum, and marrow about 33 percent; the lung, pancreas, muscle, and stomach, 16 percent; the thyroid and skin, 16 percent, and the brain 5 percent of the As in the liver. Unfortunately, no blood values were determined. Similar ^{76}As distribution studies 24 hr postinjection in rabbits and rats differed so widely as not to be comparable.

Arsenic-76 excretion values determined in two other cancer patients showed total excretion of 60 percent of the intravenously injected dose at 6 days in one, 67 percent in the other at 7 days; 26 and 35 percent was excreted, respectively, in the first two days.

Marked differences in ^{76}As excretion from that in man at 48 hr was found in rabbits (70 percent) and rats (<10 percent) compared with the 26 and 35 percent in man (117).

A significant difference in metabolism between inorganic and organic As has been demonstrated in growing rats (118). Rats fed livers of turkey fed an organically (protein) bound *p*-ureidobenzene arsonic acid excreted more (4 percent) of the organically bound As than did those fed As_2O_3, although both sources gave rise to significant tissue storage (11 and 15 percent); the urine:fecal excretion ratio was about 1 for the organic source, but more than 2 for the inorganic source. These results are in general, but not quantitative, agreement with those of Coulson et al. (119) and Overby and Frost (120).

Normal urinary values, expressed as total As, vary greatly depending on dietary sources, and probably on analytic method. Schrenk and Schreibeis (121) compared their results with those of past investigators (111, 115) and concluded that normal urinary As values for the majority are <0.1 mg/liter, with a few being >0.2, unless some unusual dietary intake of As occurred. (Those eating seafood had values ranging from 0.12 to 1.5 mg As/liter; those not eating seafood, from 0.02 to 0.16.) Determinations of normal urinary As values in 14 foreign countries, including three in South America, four in western Europe, three in eastern Europe, Egypt, and Japan, are in general agreement with the conclusions of Schrenk and Schreibeis (121); only 3.3 percent of 631 specimens analyzed had >100 μg As/liter (122).

In connection with the results of past determinations of urinary As, dating back to 1916, it should be noted that there has been considerable improvement in the accuracy and the sensitivity of the methods, the Marsh test before 1930, the Gutzeit test up until about 1950, the molybdenum blue method after 1950, and lately, atomic absorption of AsH_3. For evaluation of industrial exposures, an analytic method that will differentiate between inorganic and organic As is needed. Attempts along this line have so far been unsuccessful.

Arsenic determined in the hair of workers making solutions of sodium arsenite showed values of 108, 85, and 64 ppm depending upon worker category, compared with 13 ppm in unexposed controls, with values in a few of the workers between 200 and 500 ppm. These values seem high compared with those reported by other investigators (124); the hair specimens may have been externally contaminated. Young and Rice (125) reported that they were unable to distinguish between As deposited externally and internally in the hair.

Although blood As values have been determined in the past (126, 127), no use of this procedure has been made in the United States to evaluate worker exposure.

The *mode of action* of As envisioned as early as 1909 by Ehrlich (128) to involve thiol groups (SH) was later (1923) definitely shown to combine with the biologically active SH-containing substances cysteine and glutathione (GSH) by Voegtlin (129). Subsequently, specific enzyme systems, pyruvic acid oxidase, (130) D-amino acid oxidase, 2-glutamic acid oxidase, monoamine oxidase, liver choline oxidase, glucose oxidase, and transaminases, shown to be inhibited by As^{3+}, were reactivated by GSH (131). The more intimate mode of action of As^{3+}, and basis for the therapeutic effectiveness of BAL (British anti-lewisite), 2,3-dimercaptopropanol, was further defined in 1953 by Gunsalus (132), who showed that lipoic acid, 6,8-dithiooctanoic acid, an essential

coenzyme for the multienzyme pyruvic dehydrogenase complex, was a cyclic disulfide with which As^{3+} froms an As-mercaptide ring. This ring can be cleaved, and lipoic acid regenerated by added SH groups, such as those of BAL.

More recently, the role of selenium (Se) has emerged as even more critical than sulfur (S) in the mode of action of As^{3+}, particularly with regard to theories on the development of arsenical cancers (133). Its greatly lower terrestrial (Se : S ratio 1 : 6000–30,000) (134) and hence body content substantiates its criticality, for GSH peroxidase (GSH-Px) has been shown to be a Se-dependent enzyme (135). GSH-Px is essential to the maintenance of red blood cell integrity, among other functions. Because irreversible copper, silver, and gold complexes with GSH-Px from traces of these elements have been demonstrated (136), the possibility of such action by As^{3+} is suggested. In this way body stores of enzymatically active selenium would be depleted. Coupling this with the increasing evidence for the pivotal role of Se in cancer prevention (137), a rational explanation is offered for development or lack of development of As hyperkeratosis and cancers, depending on the relative amounts of Se and As. This concept could account for the inability of investigators to elicit cancers in animals with As compounds (138, 139); commercial animal diets are two- to threefold richer in Se than human diets.

BAL Therapy. As mentioned above, the finding that the mode of action of As^{3+} involved combination with SH groups, in which two SH groups combine with one As, led to the development of the therapeutic agent BAL, 2,3-dimercaptopropanol. BAL, being a dithiol, forms cyclic dithioarsenites which are more stable than the protein-SH arsenites and are thus capable of eliminating excess As from the body.

Pinto and McGee (115) have given a detailed description of their experience with BAL in the treatment of acute chemical dermatitis. It can be summarized as follows. BAL is injected intramuscularly in hospitalized patients (for convenience, not necessity) in doses of 1.5 to 1.6 ml, every 6 hr day and night, and urinary As excretion followed for 3 to 6 days. BAL injection stimulated As excretion for the first 3 days, then gradually decreased to a slower rate of elimination to the sixth day, with an average daily excretion during the 6-day treatment of about 0.7 mg As per patient. Rapid improvement of skin irritation as well as relief from itching and other specific symptoms were attributed to the specific BAL therapy.

The authors pointed out some disadvantages of the procedure. The first few injections may be painful with systemic reactions of mild shock. These can be alleviated by prior injection of epinephrine. Care must be taken to avoid exposure of the nerve; sciatic nerve exposure in one case resulted in a neuritis that persisted for several months.

Heyman et al (140), however, found no dramatic improvement in 22 patients with arsenical peripheral neuropathy when treated with BAL for 6 to 8 weeks after As exposure, in agreement with two similar cases in the literature. But early treatment with BAL did not prevent development of peripheral neuropathy. No adverse effects of BAL treatment were noted, however.

Epidemiology and Carcinogenicity. About 16 epidemiologic studies of sorts have been reported, beginning with that of Hill and Faning in 1948 in England (123) and

concluding in 1975 with those of Newman and Archer et al. (141) and Enterline (142). Eight of these were published between 1969 and 1975, a period when more sophisticated statistical procedures and more searching and more critical evaluations were made than formerly, with a fuller appreciation of other environmental factors that may have promoted arsenical cancers. Before 1969, for example, tobacco smoking was not considered in any of the studies, because smoking as a respiratory or cardiovascular risk had not been firmly established or fully appreciated. Similarly, the contributions of associated exposures of irritant acid gases and of trace elements from the smelting process were not given proper consideration. Another deficiency in some reports was the failure to include those who had left employment before retirement. Such oversight considerably reduces the value and the validity of those studies dealing with carcinogenic risk reported through 1963.

Mortality surveys have been made in five areas: (1) copper smelting, (2) orchard spraying, (3) production of arsenicals, (4) grapevine growing, and (5) sheepdipping. Although surveys in these areas focused mainly on deaths from respiratory cancer, dermatitis, perforation of the nasal septum, turbinate inflammation, pharyngitis, and conjunctivitis were also reported by Pinto and Bennett (143), and Roth (144) reported "As cirrhosis," hemangiosarcomas, as well as dermal cancers and cancers at other sites among German grape growers. Pinto and Bennett stated that dermatitis occurred in 80 percent of those workers with urinary As values between 1 and 3 mg/liter, and in 100 percent of those with values >3 mg/liter.

In summarizing the evidence for As carcinogenicity, a selection has been made to include those reports that have given consideration to smoking and other associated exposure factors. In this regard, analyses of the mortality experience of smelters at a copper plant have been updated to 1975 (143). Statistically significant ($P < .05$) excesses in respiratory cancer (SMR, 300 observed vs. 160 to 164 expected) were found among 530 retired workers at ages over 65 for the period January 1, 1949 through December 31, 1973. If this was related to an intensity index of exposure, it was found that workers with a urinary As value of <200 μg/liter and exposed <25 years have no excess respiratory cancer. For those exposed 25 years or more, all excess cancer deaths are statistically significant and are related to the intensity of exposure as measured by urinary As. All relationships were almost perfectly linear, with the SMRs showing a 0.98 correlation.

From smoking histories of 377 workers alive on January 1, 1961, smokers 65 years and older have a risk of respiratory cancer fivefold greater than nonsmokers (using the definition of a nonsmoker as one who has not smoked in the preceding 10 years). The added risk imposed by As exposure is 822/100,000 per year compared with 371/100,000 per year for nonsmokers. Smokers had a slightly greater As exposure at retirement than nonsmokers, but this was not sufficient, it was felt, to account for the added number of deaths.

In another study of 8,047 white, male workers in a number of other copper smelters dying between 1938 and 1963, Lee and Fraumeni (145) gave attention not only to the degree and duration of As exposure, but also to associated metal exposures. As exposures were classed as heavy, medium, and light according to urinary As values, and also classified according to years of smelter work, cohort 1, 15 or more years completed

before 1938; cohort 2, 15 or more years completed between 1938 and 1963; cohort 3, 10 to 14 years; cohort 4, 5 to 9 years; and cohort 5, 1 to 4 years. When the mortality statistics were compared with those of the white, male population of the respective states in which the mills were located, specific causes of death significantly elevated were respiratory cancer, diseases of the heart, cirrhosis of the liver, and tuberculosis. Respiratory cancer increased in all five cohorts, and oddly, cardiac disease increased in all but cohort 1; the investigators give no explanation. Excess respiratory cancer deaths were as high as eightfold in workers having more than 15 years at high As exposure, and greatest risk of respiratory cancer mortality was found in workers with heaviest or moderate SO_2 and heaviest As exposures. Unfortunately no smoking histories were obtained. However, among the 317 smelter workers exposed heavily to ferromanganese dust, five respiratory cancer deaths occurred, a number greater than expected, and none of these deaths occurred in workers with heavy As exposures. But two of the five had heavy SO_2 exposure and one had heavy SiO_2 exposure. The authors made for the first time the important observations that, although the findings support the hypothesis that inhaled As (As_2O_3) is a respiratory carcinogen in man, an influence of SO_2 or unidentified chemicals, varying concomitantly with As exposure, cannot be discounted.

The influence of smoking habits on lung cancer mortality in employees of a Utah Division of a copper company who died between 1959 and 1964 was investigated by Rencher and Carter (146). Smoking habits were ascertained for all deceased smelter workers and randomly for mine and concentrator workers. The percentages of smokers at the smelter, mine, and concentrator were approximately the same (60 percent) but the percentage of lung cancer deaths of the total deaths was higher (9.2) among the smelters who smoked than among those that did not (3.3). Smoking miners and concentrators had the same percentage of lung cancer deaths, 3.3, which is the age-adjusted cancer death rate for the state. Nonsmoking miner and concentrator lung cancer deaths were well below the state average, 0.7 and 0.8 percent, respectively.

When lung cancer deaths were related to average exposures for five exposure indexes, SO_2, H_2SO_4, Cu, Pb, and As, all five cumulative exposure indexes were substantially higher for the lung cancer group. For smelters, the average duration of exposure was approximately 29 years.

Thus this study (146) again introduces strong evidence that tobacco smoking and exposure to other agents associated with copper ore smelting promote As lung cancers after an exposure period of nearly 30 years (average age at death, 59 to 64.9 years) provided exposure concentrations are sufficiently high. (Stack emission data dating back to 1944 indicate exposure concentrations at least three times higher before 1959 than after.)

Four additional epidemiologic studies were made from 1973 to 1975 (147–150). Each study either reported finding increased respiratory cancer from copper ore smelting (147) or from As insecticide production (148, 149), or upon reexamination using independent data sources by NIOSH (151) found excess respiratory cancer mortality whereas previous investigators had found As insecticide exposure beneficial to health (150). It should be particularly noted that the studies on As insecticide production and use (spraying) involved, in addition to As_2O_3, exposures to arsenates of Pb, Ca, and Mg

and to copper acetoarsenite (149, 150) or to mixtures of them. Copper acetoarsenite (along with sodium arsenite and Pb and Ca arsenates) figured prominently in the insecticide discussed in Reference 148, with exposures in excess of 5 mg As/m^3 until the late 1940s.

Finally, in implicating As as a carcinogen for man, a number of items emerge from the metabolic and epidemiologic studies just summarized that bring into sharper focus what appears to be the actual role of As in cancers from industrial exposures. First, As compounds vary greatly in their capacity to initiate human cancer. As a prominent example, there is no evidence that As_2O_3 per se can induce respiratory cancer in either humans or animals; promoters in the form of smoking or as irritant acid gases, and/or associated metals, Cu, Fe, and Pb, have been identified with excesses of respiratory cancer (145–147); when such promoters are absent, mortality from respiratory cancer shows no excesses over statewide rates. Further substantiation of this assertion is the lack of demonstrated As_2O_3 cancers in animals not exposed to these promoters (138, 139) and the observation of higher dietary intake of Se by animals than by humans without cancer production (136). A second factor, overlooked in past, highly uncritical reviews (151), is the pinpointing of certain arsenicals that can apparently elicit respiratory cancer without promoters; copper acetoarsenite (Paris green) (123, 149) and lead arsenate (148, 150) are two such compounds. Third, those arsenicals, whether requiring promoters or not, must be classed as human carcinogens of low potency; five independent investigators (123, 145, 146, 149, 152) estimated the latent period of exposure to be between 35 and 41 years at exposure levels well above the then-permissible TLV of 0.15 mg As/m^3.

3.6 Hygienic Standards

The Threshold Limits Committee of the American Conference of Governmental Industrial Hygienists, recognizing the distinctly different health hazards associated with As_2O_3 production and its handling and use, recommended in 1975 a TLV for As_2O_3 production of 0.05 mg As/m^3 with the carcinogenic classification of Ala, and with the proviso that Sb_2O_3 and SO_2 be kept below a ceiling of 0.05 mg Sb/m^3 and 5 ppm SO_2. The Ala designation refers to a carcinogenic classification for those substances proven carcinogenic for workers and for which a TLV has been assigned. For As_2O_3, handling and use, a TLV of 0.25 mg As/m^3 was recommended.

A NIOSH criteria document, issued in 1973, recommended especially the same limit as that for As_2O_3 production of 0.05 mg As/m^3 for "arsenic." In 1975, a revised and updated NIOSH document recommended an air standard of 0.002 mg As/m^3, again making no distinction between health hazards associated with different types of exposure.

3.7 Arsine, AsH_3

Arsine is a colorless, flammable gas with a garlic-like odor, now believed to be attributable to its tellurium content. AsH_3 deposits As on exposure to light and moisture.