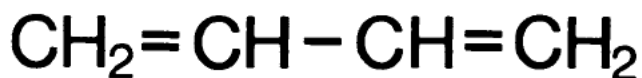


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1,3 - Butadiene



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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FOREWORD

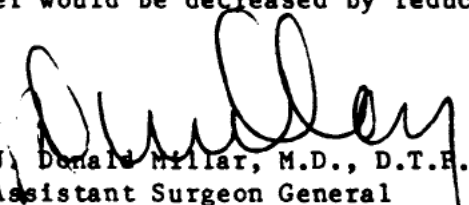
Current Intelligence Bulletins are reports issued by the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control, Atlanta, Georgia, for the purpose of disseminating new scientific information about occupational hazards. A Current Intelligence Bulletin may draw attention to a hazard previously unrecognized or may report new data suggesting that a known hazard is either more or less dangerous than was previously thought.

Current Intelligence Bulletins are prepared by the staff of the Division of Standards Development and Technology Transfer, NIOSH, (Robert A. Taft Laboratories, 4676 Columbia Parkway, Cincinnati, Ohio, 45226) and are distributed to representatives of organized labor, industry, public health agencies, academic institutions, and public interest groups as well as to those federal agencies, such as the Department of Labor, which have responsibilities for protecting the health of workers. It is our intention that anyone with the need to know should have ready access to the information contained in these documents; we welcome suggestions concerning their content, style, and distribution.

It is recommended that 1,3-butadiene be regarded as a potential occupational carcinogen, teratogen, and as a possible reproductive hazard. Consequently, appropriate engineering and work practice controls should be used to reduce worker exposure. These recommendations are based on long-term animal studies which demonstrated carcinogenicity, teratogenicity and adverse effects upon the testes and ovaries.

On the basis of this information, it is recommended that producers and users of 1,3-butadiene disseminate this information to their workers and customers and that professional and trade associations and unions inform their members of the potential hazards of working with 1,3-butadiene.

It is also recommended that the present Occupational Safety and Health Administration (OSHA) standard of 1,000 ppm for exposure to 1,3-butadiene be reexamined. The excess risk of cancer to workers exposed to specific airborne concentrations of 1,3-butadiene has not yet been determined, but the probability of developing cancer would be decreased by reducing exposure.



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CURRENT INTELLIGENCE BULLETIN #41

1,3-BUTADIENE

FEBRUARY 9, 1984

ABSTRACT

Inhalation exposure of rats and mice to 1,3-butadiene induced a carcinogenic response at multiple sites. Mammary fibroadenomas/carcinomas, uterine sarcomas, Leydig cell adenomas of the testes, thyroid follicular cell adenomas, exocrine tumors of the pancreas, and Zymbal gland carcinomas were identified in rats exposed at concentrations of 1,000 or 8,000 ppm of 1,3-butadiene. Mice exposed to 625 or 1,250 ppm of 1,3-butadiene developed a high incidence of malignant lymphomas; an increased incidence of other tumors, including hemangiosarcoma; and testicular and ovarian atrophy.

The offspring of pregnant rats exposed to 1,3-butadiene at 8,000 ppm had major skeletal defects. In addition, fetal toxicity was observed when pregnant dams were exposed at 200 ppm, 1,000 ppm, and 8,000 ppm.

Epidemiological studies of workers employed in facilities producing styrene-butadiene rubber indicated an increased, but not statistically significant, risk of mortality from neoplasms of the lymphatic and hematopoietic tissues and from leukemia.

Based on these data, the National Institute for Occupational Safety and Health (NIOSH) recommends that 1,3-butadiene be regarded as a potential occupational carcinogen and teratogen and as a possible reproductive hazard.

BACKGROUND

Physical and Chemical Properties

1,3-Butadiene is a colorless, noncorrosive, flammable gas. It is slightly soluble in water, more soluble in methanol and ethanol, and readily soluble in common organic solvents such as cyclohexane. Additional chemical and physical properties are listed in Table 1.

Table 1. Chemical and Physical Properties [1-3]

Chemical Identity: 1,3-Butadiene

CAS Registry No.: 106-99-0

Synonyms: Biethylene, bivinyl, butadiene, buta-1,3-diene,
alpha-gamma-butadiene, divinyl, erythrene, NCI-C50602,
pyrrolylene, vinylethylene

Molecular Weight: 54.10

Molecular Formula: C_4H_6

Structural Formula: $CH_2:CHCH:CH_2$

Boiling point -4.41°C (at 760 mmHg)

Freezing point: -108.9°C

Heat of vaporization, 389 (93)
J/g (cal/g), 25°C

Explosive limits, vol %
butadiene in air
lower 2.0
upper 11.5

Vapor pressure 2 atm at 15.3°C
5 atm at 47.0°C

Recognition (Odor)
Threshold 1.3 ppm

Production, Use, and Potential for Occupational Exposure

In the United States (U.S.), approximately 78% (3,240 million pounds) of all 1,3-butadiene is produced as a coproduct in the manufacture of ethylene, and 22% (910 million pounds) is produced by dehydrogenation of n-butene and n-butane [4].

Styrene-butadiene rubber (SBR) and polybutadiene rubber (BR) account for the two largest uses of 1,3-butadiene in the U.S., approximately 2,880 million pounds (primarily in the tire industry); polychloroprene (neoprene) rubber

production ranks third, 320 million pounds. Other uses are in styrene-butadiene copolymer latexes used as carpet backing and paper coating materials; in acrylonitrile-butadiene-styrene (ABS) resins used to make high impact resistant pipes and parts for automobiles and appliances; and in the production of nitrile rubber, adiponitrile/hexamethylenediamine for nylon, polybutadiene polymers, thermoplastic elastomers, and methyl methacrylate-butadiene-styrene and nitrile resins. As an intermediate, 1,3-butadiene is used in the production of various chemicals such as 1,4-hexadiene, 1,5-cyclooctadiene, and fungicides such as tetrahydrophthalic anhydride [4].

Approximately 65,000 workers (Table 2) are potentially exposed to 1,3-butadiene as estimated from data compiled from the National Institute for Occupational Safety and Health (NIOSH) National Occupational Hazard Survey (NOHS) [5].

Table 2. Number of Workers Potentially Exposed by Industry

SIC* Code	Description	Workers Potentially Exposed
26	Paper and allied products	1,221
28	Chemical and allied products	44,980
29	Petroleum and coal products	84
30	Rubber and plastics products, NEC	9,086
33	Primary metal industries	55
34	Fabricated metal products	96
35	Machinery, except electrical	1,210
36	Electrical equipment and supplies	121
37	Transportation equipment	145
38	Instruments and related products	175
39	Miscellaneous manufacturing industries	2,244
73	Miscellaneous business services	5,339
80	Medical and other health services	493

*Standard Industrial Classification Code

Health Hazard Evaluation surveys conducted by NIOSH at six facilities indicated that exposures to 1,3-butadiene in those facilities were significantly below the OSHA standard of 1,000 ppm. The range of reported exposures was 0.06 ppm to 39 ppm. The types of facilities surveyed included those which manufactured helmets and visors, synthetic rubber, rubber tires and tubes, automotive weather stripping, braided hoses, and plastic components for aircraft [6-11].

EXPOSURE STANDARDS AND GUIDES

Based on the 1968 Threshold Limit Value (TLV®) of the American Conference of Governmental Industrial Hygienists [12], the Occupational Safety and Health Administration (OSHA) promulgated a standard for occupational exposure to 1,3-butadiene of 1,000 ppm (2,200 mg/m³) determined as an 8-hour time-weighted average (TWA) concentration [13]. The TLV® of 1,000 ppm was based on the absence of significant progressive injury to rats and guinea pigs exposed at 600, 2,300, or 6,700 ppm of 1,3-butadiene during an 8-month daily exposure period and only mild irritation experienced by human subjects exposed at 8,000 ppm [12].

The ACGIH included 1,3-butadiene in their Notice of Intended Changes for the 1983-84 Threshold Limit Values, based upon reported animal carcinogenicity data. The Intended Change identified 1,3-butadiene as an industrial substance suspect of carcinogenic potential for man. No numerical TLV® was assigned [14].

TOXICITY

Results of Animal Studies

Acute -- Inhalation exposure studies with 1,3-butadiene have shown the lethal concentration for 50 percent (LC₅₀) of the mice and rats tested to be 122,000 ppm and 129,000 ppm, respectively, [15]; an LC₁₀₀ of 250,000 ppm was reported for rabbits exposed to 1,3-butadiene [16]. Toxic effects of exposure in the animals progressed from light anesthesia, to running movements and tremors, to deep anesthesia and death.

Subchronic -- Except for moderately increased salivation at 4,000 and 8,000 ppm concentrations, exposure of rats on a daily basis for 3 months at 1,3-butadiene concentrations of 1,000, 2,000, 4,000, or 8,000 ppm produced no effects in the animals related to the exposures [16]. Rats and guinea pigs exposed daily for 8 months at a 6,700 ppm concentration of 1,3-butadiene experienced a slightly reduced body-weight gain compared to controls. No significant effects were noted in animals exposed at concentrations of 600 or 2,300 ppm [17].

Chronic -- In a chronic inhalation study, rats exposed for two years, 6 hours per day, 5 days per week at 1,3-butadiene concentrations of 1,000 or 8,000 ppm developed tumors at multiple sites. Occurrences of mammary fibroadenomas/carcinomas, thyroid follicular cell adenomas, and uterine stromal sarcomas in female rats exposed at both concentrations were statistically significant when compared with the controls. Male rats had

significant increases in the incidence of testicular Leydig cell adenomas at 1,000 ppm and 8,000 ppm exposures and for pancreatic exocrine tumors at 8,000 ppm when compared with the controls [18].

Mice exposed at 1,3-butadiene concentrations of 625 or 1,250 ppm, 6 hours per day, 5 days per week for 61 weeks developed cancer at multiple sites. A statistically significant increase of tumors in exposed male and female mice compared to the controls included hemangiosarcomas of the heart, malignant lymphomas, papillomas of the stomach, and alveolar/bronchiolar adenomas and carcinomas of the lungs. Exposed female mice also had a statistically significant increase of granulomatous tumors of the ovary at exposures of 625 and 1,250 ppm and mammary gland carcinomas at a concentration of 8,000 ppm when compared with the controls. In addition, 1,3-butadiene was associated with the induction and early onset of non-neoplastic changes in both sexes of mice. These non-neoplastic changes included atrophy of the ovaries, testes, and nasal olfactory epithelium; hyperplasia and metaplasia of the respiratory epithelium; and liver necrosis [19].

Teratogenicity and Reproductive Effects -- An inhalation study of pregnant Sprague-Dawley rats exposed at 200, 1,000, or 8,000 ppm of 1,3-butadiene for 6 hours per day on days 6-15 of gestation produced dose-related maternal and fetal toxicity when compared to an unexposed group of controls. Depressed body weight gain among dams was observed at all concentrations, and fetal growth was significantly retarded among rats exposed at the 8,000 ppm. Fetal deaths, though not statistically significant, were higher for all exposed groups, and at 8,000 ppm, a statistically significant increase in major skeletal abnormalities was recorded (skull, spine, sternum, long bones and ribs) [20].

Mutagenicity -- 1,3-Butadiene was not found to be a direct-acting mutagen, but in the presence of a liver microsomal activating system, it was transformed into mutagenic metabolites [21].

HUMAN HEALTH EFFECTS

Acute Effects

Occupational exposure at 2,000, 4,000 or 8,000 ppm concentrations of 1,3-butadiene is reported to cause irritation of the skin, eyes, nose, and throat. Coughing, drowsiness, and fatigue have also been reported at higher, but not specified, exposure concentrations. These physiological responses dissipated upon removal of the workers from the area where 1,3-butadiene had accumulated [17,22,23]. Dermatitis and frostbite may result from exposure to liquid and evaporating 1,3-butadiene [24].

Epidemiology Studies

A retrospective cohort study was conducted at two SBR production facilities in the U.S. The combined cohorts consisted of 2,756 white males who had an average length of employment of approximately 10 years. No historical exposure data were available. Environmental sampling conducted at the time of the study characterized the most likely chemical exposures to be 1,3-butadiene, styrene, and benzene. Average exposure concentrations of 1,3-butadiene in the two facilities were 1.24 ppm (range, 0.11-4.17 ppm) and 13.5 ppm (range, 0.34-174 ppm). No statistically significant excesses in total or cause-specific mortality were observed for the total worker populations of either facility. However, a subgroup of workers from one cohort had a non-statistically significant excess mortality for cause-specific categories of the lymphatic and hematopoietic tissues [25].

Eight facilities that produced SBR in the U.S. and Canada provided data for another retrospective study [26]. The study covered a period of 36 years and included a total worker population of 13,920 black and white males. No significant excesses in cause-specific mortality were observed; however, some cancers (digestive system, kidney, lymph nodes, and larynx) occurred at a higher rate in white males compared with the general population, and the black male population had a non-statistically significant elevated risk of arteriosclerotic disease. The small number of workers in the cohorts from the 8 facilities studied and the relatively short latency periods of workers exposed inhibited the capability to identify statistically significant increases in risk of mortality or cause-specific disease. Also, environmental data were insufficient to characterize and quantify the workers' chemical exposures.

RECOMMENDATIONS

There are several classifications for identifying a substance as a carcinogen. Such classifications have been developed by the National Toxicology Program [19], the International Agency for Research on Cancer [27], and OSHA [28]. NIOSH considers the OSHA classification the most appropriate for use in identifying carcinogens in the workplace. This classification is outlined in 29 CFR 1990.103* [28]. Since exposure to

*"Potential occupational carcinogen" means any substance, or combination or mixture of substances, which causes an increased incidence of benign and/or malignant neoplasms, or a substantial decrease in the latency period between exposure and onset of neoplasms in humans or in one or more experimental mammalian species as the result of any oral, respiratory or dermal exposure, or any other exposure which results in the induction of tumors at a site other than the site of administration. This definition also includes any substance which is metabolized into one or more potential occupational carcinogens by mammals."

1,3-butadiene has been shown to produce malignant tumors in rats and mice, it meets the OSHA criteria; therefore, NIOSH recommends that 1,3-butadiene be considered a potential occupational carcinogen. In addition, there is a possible reproductive hazard to workers exposed to 1,3-butadiene based on maternal and fetal toxicity observed in 1,3-butadiene exposed rats; an indication of teratogenicity in exposed rats; and suggestion of testicular and ovarian atrophy in mice exposed to 1,3-butadiene.

NIOSH also recommends that the present OSHA standard of 1,000 ppm TWA for 1,3-butadiene be reexamined, based on the health effects in animals exposed at concentrations of 1,3-butadiene at or below the standard. In addition, the excess risk of cancer to workers exposed to specific airborne concentrations of 1,3-butadiene has not yet been determined, but the probability of developing cancer would be decreased by reducing exposure. As prudent public health policy, employers should voluntarily assess the conditions under which workers may be exposed to 1,3-butadiene and to the fullest extent possible take all reasonable precautions to reduce exposure.

Guidelines recommended in the Appendix for minimizing worker exposure to 1,3-butadiene are general in nature and should be adapted to specific work situations as required.

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APPENDIX

GUIDELINES FOR MINIMIZING EMPLOYEE EXPOSURE TO 1,3-BUTADIENE

It is recommended that 1,3-butadiene be regarded as a potential occupational carcinogen and teratogen and as a possible reproductive hazard. These recommendations are based on long-term animal studies which demonstrated carcinogenicity, teratogenicity and adverse effects upon the testes and ovaries. Consequently, appropriate engineering and work practice controls should be used to reduce worker exposure to the fullest extent feasible. The area in which 1,3-butadiene is used should be restricted to only those employees essential to the process or operation. The guidelines listed below are general in nature and should be adapted to specific work situations as required.

EXPOSURE MONITORING

Initial and routine worker exposure surveys should be made by competent industrial hygiene and engineering personnel. These surveys are necessary to determine the extent of worker exposure and to ensure that controls already in place are operational and effective. NIOSH's Occupational Exposure Sampling Strategy Manual may be helpful in developing efficient programs to monitor worker exposure to 1,3-butadiene [29]. The manual discusses how to determine the need for exposure measurements and select sampling times.

Worker exposures should be estimated by 8-hour TWA and short-term (15-minute) exposures calculated from personal or breathing zone samples. Short-term samples should be taken during periods of maximum expected exposure by using all available knowledge of the work areas, procedures, and processes. Area and source measurements may be useful in identifying problem areas, processes, and operations.

A detailed analytical method for 1,3-butadiene is in the NIOSH Manual of Analytical Methods, Second Edition [30].

CONTROLLING WORKER EXPOSURE

There are four basic methods of limiting worker exposure to 1,3-butadiene, none of which is a simple industrial hygiene or management decision. Careful planning and thought should be used prior to implementation.

Product Substitution

Substitution, when feasible, of an alternative material with a lower potential health risk is an important method for reducing exposure. Extreme care must be used when selecting substitutes. Possible health effects from potential exposure to alternatives for 1,3-butadiene should be fully evaluated prior to selection.

Contaminant Controls

Airborne concentrations of 1,3-butadiene can be most effectively controlled at the source of contamination by enclosure of the operation and use of local exhaust ventilation. Guidelines for selected processes and operations can be found in NIOSH's Recommended Industrial Ventilation Guidelines [31]. When a process or operation is being enclosed, a slight vacuum should be used to create negative pressure so that leakage will cause external air to flow into the enclosure and minimize contamination of the workplace. This can be accomplished with a well-designed local exhaust ventilation system that physically encloses the process as much as possible with sufficient capture velocity to keep the contaminant from entering the workplace atmosphere. The design of ventilation systems should take into account the reactive characteristics of 1,3-butadiene.

Ventilation equipment should be checked at least every three months to ensure adequate performance. System effectiveness should also be checked soon after any change in production, process, or control that might result in significant increases in airborne exposure to 1,3-butadiene.

Worker Isolation

If feasible, workers may be isolated from direct contact with the work environment by the use of automated equipment operated from a closed control booth or room. The control room should be maintained at a greater air pressure than that surrounding the process equipment so that air flows out of, rather than into, the room. This type of control will not protect workers who must perform process checks, adjustments, maintenance, assembly-line tasks, and related operations. Therefore, special precautions are often necessary to prevent or limit worker exposure in these situations and frequently involve the use of personal protective equipment.

Personal Protective Equipment

Personal protective equipment, which may include goggles, gloves, coveralls, footwear, and respirators, should not be the only means of preventing or

minimizing exposure during routine operations. Since 1,3-butadiene is a skin irritant and can produce frostbite, personal protective clothing and equipment should be selected that is appropriate for the potential exposures.

The use of respiratory protection requires that a respiratory protection program be instituted according to the requirements of 29 CFR 1910.134 [32] and that the respirators have been approved by the Mine Safety and Health Administration (MSHA) and by NIOSH. This program should include training on proper fit testing and use and procedures for respirator maintenance, inspection, cleaning and evaluation.

MEDICAL SURVEILLANCE

A medical surveillance program should be made available that can evaluate both the acute and chronic effects of 1,3-butadiene exposure. Effects such as upper respiratory irritation, dermatitis, and irritation should alert management that unacceptable acute exposure to 1,3-butadiene may be occurring. A careful history should be taken initially and updated yearly. Unusual medical findings for a worker should prompt medical personnel to consider specific tests for the individual.

CUMULATIVE LIST OF NIOSH CURRENT INTELLIGENCE BULLETINS

1.	Chloroprene	- January 20, 1975
2.	Trichloroethylene (TCE)	- June 6, 1975
3.	Ethylene Dibromide (EDB)	- July 7, 1975
4.	Chrome Pigment	- June 24, 1975 - October 7, 1975 - October 8, 1976
5.	Asbestos - Asbestos Exposure during Servicing of Motor Vehicle Brake and Clutch Assemblies	- August 8, 1975
6.	Hexamethylphosphoric Triamide (HMPA)	- October 24, 1975
7.	Polychlorinated Biphenyls (PCB's)	- November 3, 1975 - August 20, 1976
8.	4,4'-Diaminodiphenylmethane (DDM)	- January 30, 1976
9.	Chloroform	- March 15, 1976
10.	Radon Daughters	- May 11, 1976
11.	Dimethylcarbamoyl Chloride (DMCC) Revised	- July 7, 1976
12.	Diethylcarbamoyl Chloride (DECC)	- July 7, 1976
13.	Explosive Azide Hazard	- August 16, 1976
14.	Inorganic Arsenic - Respiratory Protection	- September 27, 1976 - October 6, 1976
15.	Nitrosamines in Cutting Fluids	
16.	Metabolic Precursors of a Known Human Carcinogen, Beta-Naphthylamine	- December 17, 1976
17.	2-Nitropropane	- April 25, 1977
18.	Acrylonitrile	- July 1, 1977
19.	2,4-Diaminoanisole in Hair and Fur Dyes	- January 13, 1978
20.	Tetrachloroethylene (Perchloroethylene)	- January 20, 1978
21.	Trimellitic Anhydride (TMA)	- February 3, 1978
22.	Ethylene Thiourea (ETU)	- April 11, 1978
23.	Ethylene Dibromide and Disulfiram Toxic Interaction	- April 11, 1978
24.	Direct Black 38, Direct Blue 6, and Direct Brown 95 Benzidine Derived Dyes	- April 17, 1978
25.	Ethylene Dichloride (1,2-Dichloroethane)	- April 19, 1978
26.	NIAX Catalyst ESN	- May 22, 1978
27.	Chloroethanes - Review of Toxicity	- August 21, 1978
28.	Vinyl Halides - Carcinogenicity	- September 21, 1978
29.	Glycidyl Ethers	- October 12, 1978
30.	Epichlorohydrin	- October 12, 1978
31.	Adverse Health Effects of Smoking and the Occupational Environment	- February 5, 1979
32.	Arsine (Arsenic Hydride) Poisoning in the Workplace	- August 3, 1979

CUMULATIVE LIST OF NIOSH CURRENT INTELLIGENCE BULLETINS (CONTINUED)

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| 33. | Radiofrequency (RF) Sealers and Heaters:
Potential Health Hazards and Their Prevention | - December 4, 1979 |
| 34. | Formaldehyde: Evidence of Carcinogenicity | - April 15, 1981 |
| 35. | Ethylene Oxide (EtO): Evidence of
Carcinogenicity | - May 22, 1981 |
| 36. | Silica Flour: Silicosis | - June 30, 1981 |
| 37. | Ethylene Dibromide (EDB)
Revised | - October 26, 1981 |
| 38. | Vibration Syndrome | - March 29, 1983 |
| 39. | The Glycol Ethers, with Particular
Reference to 2-Methoxyethanol and
2-Ethoxyethanol: Evidence of Adverse
Reproductive Effects | - May 2, 1983 |
| 40. | 2,3,7,8-Tetrachlorodibenzo-p-dioxin
(TCDD, "Dioxin") | - January 23, 1984 |
| 41. | 1,3-Butadiene | - February 9, 1984 |

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