

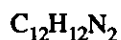
# OCCUPATIONAL SAFETY AND HEALTH GUIDELINE FOR BENZIDINE

## INTRODUCTION

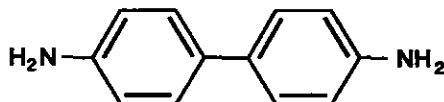
This guideline summarizes pertinent information about benzidine for workers and employers as well as for physicians, industrial hygienists, and other occupational safety and health professionals who may need such information to conduct effective occupational safety and health programs. Recommendations may be superseded by new developments in these fields; readers are therefore advised to regard these recommendations as general guidelines and to determine periodically whether new information is available.

## SUBSTANCE IDENTIFICATION

### • Formula



### • Structure



### • Synonyms

1,1'-Biphenyl-4,4'-diamine, 4,4'-diaminobiphenyl, 4,4'-biphenyldiamine, 4,4'-bianiline, C.I. Azoic Diazo Component 112, Fast Corinth base B, p-diaminodiphenyl

### • Identifiers

1. CAS No.: 92-87-5
2. RTECS No.: DC9625000

3. DOT UN: 1885 53

4. DOT label: Poison

### • Appearance and odor

Benzidine is a white, gray-yellow, or slightly reddish crystalline solid or powder that has no odor. Benzidine is no longer manufactured commercially in the United States, although this substance is still used as an intermediate.

## CHEMICAL AND PHYSICAL PROPERTIES

### • Physical data

1. Molecular weight: 184.2
2. Boiling point (at 760 mm Hg): 400°C (752°F)
3. Specific gravity (water = 1): 1.25 at 20°C (68°F)
4. Vapor density (air = 1 at boiling point of benzidine): 6.36
5. Melting point: 115°C (239°F)
6. Vapor pressure at 20°C (68°F): Quantitative data are not available, but vapor pressure is reported to be low.
7. Solubility: Slightly soluble in cold water; soluble in hot water, alcohol, and ether
8. Evaporation rate: Data not available

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Centers for Disease Control and Prevention  
National Institute for Occupational Safety and Health  
Education and Information Division

U.S. DEPARTMENT OF LABOR  
Occupational Safety and Health Administration

- **Reactivity**

1. Conditions contributing to instability: None reported
2. Incompatibilities: Contact of benzidine with red fuming nitric acid may cause a fire.
3. Hazardous decomposition products: Toxic gases and vapors (such as oxides of nitrogen, carbon monoxide, and benzidine vapors) may be released when benzidine is heated to decomposition.
4. Special precautions: None reported

- **Flammability**

The National Fire Protection Association has not assigned a flammability rating for benzidine. Benzidine may burn, but it does not ignite readily.

1. Flash point: Data not available
2. Autoignition temperature: Data not available
3. Flammable limits in air: Data not available
4. Extinguishant: Use dry chemical, carbon dioxide, water spray, or standard foam to fight fires involving benzidine.

Fires involving benzidine should be fought upwind from the maximum distance possible. Isolate the hazard area and deny access to unnecessary personnel. Emergency personnel should stay out of low areas. Containers of benzidine should be moved from the fire area if it is possible to do so safely. If this is not possible, cool containers from the sides with water until well after the fire is out. Stay away from the ends of containers. Personnel should withdraw immediately if they hear a rising sound from a venting safety device or if a container becomes discolored as a result of fire. Dikes should be used to contain fire-control water for later disposal. Firefighters should wear a full set of protective clothing and self-contained breathing apparatus when fighting fires involving benzidine. Structural firefighters' protective clothing may provide limited protection against fires involving benzidine.

## EXPOSURE LIMITS

- **OSHA PEL**

Because benzidine is a recognized occupational carcinogen, the Occupational Safety and Health Administration

(OSHA) standard for benzidine does not have a numerical permissible exposure limit (PEL); instead, the standard regulates the industrial use of benzidine by requiring implementation of stringent controls wherever benzidine or solid or liquid mixtures containing 0.1% or more benzidine by weight or volume are manufactured, processed, repackaged, released, handled, or stored. This standard is codified at 29 CFR 1910.1010.

- **NIOSH REL**

The National Institute for Occupational Safety and Health (NIOSH) considers benzidine a potential human carcinogen and recommends that the above standard [29 CFR 1910.1010] be followed [NIOSH 1992].

- **ACGIH TLV**

The American Conference of Governmental Industrial Hygienists (ACGIH) has designated benzidine as an A1 substance (recognized human carcinogen). The ACGIH has also assigned benzidine a Skin notation, which indicates that the cutaneous route of exposure (including mucous membranes and eyes) contributes to overall exposure [ACGIH 1993].

- **Rationale for limits**

The OSHA, ACGIH, and NIOSH limits are based on the risk of bladder and other cancer associated with exposure to benzidine.

## HEALTH HAZARD INFORMATION

- **Routes of exposure**

Exposure to benzidine can occur through inhalation, ingestion, skin absorption, and eye or skin contact.

- **Summary of toxicology**

1. *Effects on Animals:* Benzidine is a liver toxin and a potent carcinogen in experimental animals; in carcinogenicity bioassays, this substance caused tumors of the liver, mammary gland, Zymbal gland, colon, and bladder in animals of several species. The oral LD<sub>50</sub> in rats is 309 mg/kg [NIOSH 1993]. The oral LD<sub>50</sub> in mice is 214 mg/kg [NIOSH 1993]. Benzidine has been tested for carcinogenicity in mice, rats, and hamsters by oral administration; in mice and rats by subcutaneous administration; and in rats by inhalation and by intraperitoneal administration. Except by

inhalation, benzidine caused increased incidences in tumors, both benign and malignant, in at least one sex of animal in all species tested. Oral administration in dogs also caused bladder cancers [IARC 1982]. With activation, benzidine is mutagenic in bacterial test systems [NIOSH 1993; IARC 1982]. The International Agency for Research on Cancer (IARC) has concluded that there is sufficient evidence that benzidine is an animal carcinogen [IARC 1982].

2. *Effects on Humans:* Numerous case reports and epidemiological studies in workers from many countries, including the United States, have shown that benzidine is a potent carcinogen, causing papillomas and carcinomas of the urinary tract, and especially of the urinary bladder [IARC 1972; IARC 1982]. The latency period for benzidine tumors is 2 to 42 years, with an average latency of 16 years [Proctor et al. 1988]. In one U.S. dye manufacturing facility, bladder tumors developed in 36 workers who had been exposed to benzidine over a 45-year period (1930 to 1975) [IARC 1982]. In another group of 25 U.S. workers engaged in benzidine manufacture, 13 employees were found to have bladder tumors; all five of the workers in this group who had been exposed to benzidine for more than 15 years developed bladder tumors. Airborne benzidine concentrations at this plant were estimated to have ranged from 0.005 to 17.6 mg/m<sup>3</sup> [IARC 1982]. An increase in the number of sister chromatid exchanges has also been reported in workers exposed to benzidine [IARC 1982]. The International Agency for Research on Cancer has concluded that there is sufficient evidence that benzidine is a human carcinogen [IARC 1982].

#### • Signs and symptoms of exposure

1. *Acute exposure:* No signs or symptoms for acute inhalation or dermal exposures have been reported. However, ingestion has caused nausea, vomiting, headache, mental confusion, dizziness, vertigo, methemoglobinemia, increase in the number of white blood cells, and Heinz bodies.
2. *Chronic exposure:* Chronic exposure to benzidine may cause blood in the urine (seen microscopically in early disease) and frequent and painful urination. The onset of bladder tumors may go undetected, and the disease may be in an advanced stage before any signs or symptoms appear. Despite aggressive treatment, tumors frequently recur.

#### • Emergency Procedures

<p style="text-align: center;"><b>WARNING!</b></p> <p style="text-align: center;"><b>Exposed victims may die!</b></p> <p style="text-align: center;"><b>Transport immediately to emergency medical facility!</b></p>
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Keep unconscious victims warm and on their sides to avoid choking if vomiting occurs. *Immediately* initiate the following emergency procedures, continuing them as appropriate en route to the emergency medical facility:

1. *Eye exposure:* *Immediately and thoroughly* flush the eyes with large amounts of water for at least 15 min, occasionally lifting the upper and lower eyelids.
2. *Skin exposure:* Irritation may result from exposure to particulates or concentrated solutions, vapors, mists, or aerosols of benzidine. Benzidine can be absorbed through the skin in lethal amounts! *Immediately* remove contaminated clothing and thoroughly wash contaminated skin with soap and water for at least 15 min.
3. *Inhalation exposure:* If particulates or vapors, mists, or aerosols of benzidine are inhaled, move the victim to fresh air *immediately*. Have the victim blow his or her nose or use a soft tissue to remove particulates or residues from the nostrils.

If the victim is not breathing, clean any chemical contamination from victim's lips and perform cardiopulmonary resuscitation (CPR); if breathing is difficult, give oxygen.

4. *Ingestion exposure:* Take the following steps if benzidine or any material containing it is ingested:
  - Have the victim rinse the contaminated mouth cavity several times with a fluid such as water.
  - Have the victim drink a glass (8 oz) of fluid such as water.
  - Induce vomiting by giving syrup of ipecac as directed on the package. If ipecac is unavailable, have the victim touch the back of the throat with a finger until productive vomiting ceases.

—Do *not* force an unconscious or convulsing person to drink fluid or to vomit.

5. *Rescue*: Remove an incapacitated worker from further exposure and implement appropriate emergency procedures (e.g., those listed on the material safety data sheet required by OSHA's hazard communication standard [29 CFR 1910.1200]). All workers should be familiar with emergency procedures and the location and proper use of emergency equipment.

## EXPOSURE SOURCES AND CONTROL METHODS

The following operations may involve benzidine and result in worker exposures to this substance:

- Use as an intermediate in the preparation of azo dyes and pigments
- Formerly used in forensic medicine to detect blood and other substances
- In declining use in security printing and as a stiffening agent in rubber compounding
- In declining use as a laboratory reagent

The only method that is effective in controlling worker exposures to benzidine is:

- Process enclosure

This substance should only be handled in closed systems.

Good sources of information about control methods are as follows:

1. ACGIH [1992]. *Industrial ventilation—a manual of recommended practice*. 21st ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.
2. Burton DJ [1986]. *Industrial ventilation—a self study companion*. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.
3. Alden JL, Kane JM [1982]. *Design of industrial ventilation systems*. New York, NY: Industrial Press, Inc.

4. Wadden RA, Scheff PA [1987]. *Engineering design for control of workplace hazards*. New York, NY: McGraw-Hill.

5. Plog BA [1988]. *Fundamentals of industrial hygiene*. Chicago, IL: National Safety Council.

## MEDICAL MONITORING

Workers who may be exposed to chemical hazards should be monitored in a systematic program of medical surveillance that is intended to prevent occupational injury and disease. The program should include education of employers and workers about work-related hazards, early detection of adverse health effects, and referral of workers for diagnosis and treatment. The occurrence of disease or other work-related adverse health effects should prompt immediate evaluation of primary preventive measures (e.g., industrial hygiene monitoring, engineering controls, and personal protective equipment). A medical monitoring program is intended to supplement, not replace, such measures. To place workers effectively and to detect and control work-related health effects, medical evaluations should be performed (1) before job placement, (2) periodically during the term of employment, and (3) at the time of job transfer or termination.

### • Preplacement medical evaluation

Before a worker is placed in a job with a potential for exposure to benzidine, a licensed health care professional should evaluate and document the worker's baseline health status with thorough medical, environmental, and occupational histories, a physical examination, and physiologic and laboratory tests appropriate for the anticipated occupational risks. The physician should consider whether there exist conditions associated with increased risk, including reduced immunological competence, treatment with steroids or cytotoxic agents, pregnancy, or cigarette smoking. The medical evaluation should concentrate on the function and integrity of the bladder, kidneys, liver, skin, and blood.

A preplacement medical evaluation is recommended to detect and assess medical conditions that may be aggravated or may result in increased risk when a worker is potentially exposed to benzidine. The examining physician should consider the probable frequency, intensity, and duration of exposure as well as the nature and degree of any applicable medical condition. Such condi-

tions (which should not be regarded as absolute contraindications to job placement) include a history and other findings consistent with bladder, kidney, liver, skin, and blood diseases.

- **Periodic medical examinations and biological monitoring**

Occupational health interviews and physical examinations should be performed at regular intervals during the employment period, as mandated by any applicable Federal, State, or local standard. Where no standard exists and the hazard is minimal, evaluations should be conducted every 3 to 5 years or as frequently as recommended by an experienced occupational health physician. Additional examinations may be necessary if a worker develops symptoms attributable to benzidine exposure. The interviews, examinations, and medical screening tests should focus on identifying the adverse effects of benzidine on the bladder, kidneys, liver, skin and blood. OSHA requires periodic examinations annually for workers potentially exposed to benzidine [29 CFR 1910.1010]. Suggested diagnostic tests include urinalysis every month (with particular attention to the presence of occult blood), urine cytology every 6 months, and cystoscopy as indicated. Current health status should be compared with the baseline health status of the individual worker or with expected values for a suitable reference population.

Biological monitoring involves sampling and analyzing body tissues or fluids to provide an index of exposure to a toxic substance or metabolite. Urine benzidine levels may be useful in biological monitoring to assess exposure. Average urinary benzidine concentrations in workers exposed to benzidine concentrations in the range of 7 to 11 mg/m<sup>3</sup> are reported to be 9 mg benzidine per liter of urine (mg/l). In workers exposed to benzidine concentrations of 140 to 400 mg/m<sup>3</sup>, urinary benzidine levels reportedly range from 100 to 200 mg/l. As a carcinogen, benzidine or its metabolites should not be detectable in urine or other physiological fluids.

- **Medical examinations recommended at the time of job transfer or termination**

The medical, environmental, and occupational history interviews, the physical examination, and selected physiologic or laboratory tests that were conducted at the time of placement should be repeated at the time of job transfer or termination. Any changes in the worker's health status should be compared with those expected for a suitable reference population. Because occupational exposure to benzidine may cause diseases with pro-

longed latent periods, the need for medical monitoring may extend well beyond the termination of employment.

## **WORKPLACE MONITORING AND MEASUREMENT**

A worker's exposure to airborne benzidine is determined by using a glass fiber filter coated with sulfuric acid. Samples are collected at a maximum flow rate of 1.0 liter/min until a maximum air volume of 100 liters is collected. Immediately after sampling, the filter must be transferred to a vial containing 2 ml of deionized water. Analysis is conducted by gas chromatography using an electron capture detector. The limit of detection for this procedure is 4.1 mg/m<sup>3</sup>. This method is described in Method 65 of the *OSHA Analytical Methods Manual* [OSHA 1990].

## **PERSONAL HYGIENE**

If benzidine contacts the skin, workers should flush the affected areas immediately with plenty of water for 15 min, and then wash with soap and water. Get medical help immediately.

Clothing contaminated with benzidine should be removed immediately and should then be discarded.

A worker who handles benzidine should thoroughly wash hands, forearms, and face with soap and water before eating, using tobacco products, using toilet facilities, or applying cosmetics.

Workers should not eat, drink, use tobacco products, or apply cosmetics in areas where benzidine or a solution containing benzidine is handled, processed, or stored.

## **STORAGE**

Control, handling, processing, and storing of benzidine must be performed in accordance with OSHA's standard for benzidine [29 CFR 1910.1010]. This substance should be isolated in closed systems and should be well ventilated at the points where the system is opened. Containers should be kept closed and be protected from light.

## **SPILLS**

Treat any benzidine spill as an emergency. Preplan for benzidine spills and have a trained team ready to respond in an emergency. Cleanup personnel should be clothed and

equipped in a manner that prevents any contact with benzidine.

## SPECIAL REQUIREMENTS

U.S. Environmental Protection Agency (EPA) requirements for emergency planning, reportable quantities of hazardous releases, community right-to-know, and hazardous waste management may change over time. Users are therefore advised to determine periodically whether new information is available.

### • Emergency planning requirements

Benzidine is not subject to EPA emergency planning requirements under the Superfund Amendments and Reauthorization Act (SARA) [42 USC 11022].

### • Reportable quantity requirements for hazardous releases

A hazardous substance release is defined by EPA as any spilling, pumping, pouring, emitting, emptying, discharging, injecting, escaping, leaching, dumping, or disposing into the environment (including the abandonment or discarding of contaminated containers) of hazardous substances. In the event of a release that is above the reportable quantity for that chemical, employers are required by the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [40 CFR 355.40] to notify the proper Federal, State, and local authorities.

The reportable quantity for benzidine is 1 lb. If an amount equal to or greater than this quantity is released within a 24-hr period in a manner that will expose persons outside the facility, employers are required to do the following:

- Notify the National Response Center *immediately* at (800) 424-8802 or at (202) 426-2675 in Washington, D.C. [40 CFR 302.6].
- Notify the emergency response commission of the State likely to be affected by the release [40 CFR 355.40].
- Notify the community emergency coordinator of the local emergency planning committee (or relevant local emergency response personnel) of any area likely to be affected by the release [40 CFR 355.40].

### • Community right-to-know requirements

Employers who own or operate facilities in SIC codes 20 to 39, who employ 10 or more workers, who manufacture 25,000 lb or more or otherwise use 10,000 lb or more of benzidine per calendar year are required by EPA [49 CFR 372.30] to submit a Toxic Chemical Release Inventory Form (Form R) to EPA reporting the amount of benzidine emitted or released from their facility annually.

### • Hazardous waste management requirements

EPA considers a waste to be hazardous if it exhibits any of the following characteristics: ignitability, corrosivity, reactivity, or toxicity as defined in 40 CFR 261.21-261.24. Benzidine is listed as a hazardous waste under the Resource Conservation and Recovery Act (RCRA) [42 USC 6901 et seq.], and has been assigned EPA Hazardous Waste No. U021. This substance has been banned from land disposal and may be treated by incineration. Benzidine also may be disposed of in an organometallic or organic lab pack that meets the requirements of 40 CFR 264.316 or 265.316.

Providing detailed information about the removal and disposal of specific chemicals is beyond the scope of this guideline. The U.S. Department of Transportation, EPA, and State and local regulations should be followed to ensure that removal, transport, and disposal of this substance are conducted in accordance with existing regulations. To be certain that chemical waste disposal meets EPA regulatory requirements, employers should address any questions to the RCRA hotline at (800) 424-9346 or at (202) 382-3000 in Washington, D.C. In addition, relevant State and local authorities should be contacted for information about their requirements for waste removal and disposal.

## RESPIRATORY PROTECTION

### • Conditions for respirator use

Good industrial hygiene practice requires that engineering controls be used where feasible to reduce workplace concentrations of hazardous materials to the prescribed exposure limit. However, some situations may require the use of respirators to control exposure. Respirators must be worn if the ambient concentration of benzidine exceeds prescribed exposure limits. Respirators may be used (1) before engineering controls have been installed, (2) during work operations such as maintenance or

repair activities that involve unknown exposures, (3) during operations that require entry into tanks or closed vessels, and (4) during emergencies. Workers should use only respirators that have been approved by NIOSH and the Mine Safety and Health Administration (MSHA).

- **Respiratory protection program**

Employers should institute a complete respiratory protection program that, at a minimum, complies with the requirements of OSHA's respiratory protection standard [29 CFR 1910.134]. Such a program must include respirator selection, an evaluation of the worker's ability to perform the work while wearing a respirator, the regular training of personnel, respirator fit testing, periodic workplace monitoring, and regular respirator maintenance, inspection, and cleaning. The implementation of an adequate respiratory protection program (including selection of the correct respirator) requires that a knowledgeable person be in charge of the program and that the program be evaluated regularly. For additional information about the selection and use of respirators and about the medical screening of respirator users, consult the *NIOSH Respirator Decision Logic* [NIOSH 1987b] and the *NIOSH Guide to Industrial Respiratory Protection* [NIOSH 1987a].

## **PERSONAL PROTECTIVE EQUIPMENT**

Protective clothing should be worn to prevent any skin contact with benzidine. All skin and mucous membrane contact with benzidine should be prevented by the wearing of full-body protective clothing and gloves. Eyewash fountains and emergency showers should be available within the immediate work area whenever the potential exists for eye or skin contact with benzidine. Contact lenses should not be worn if the potential exists for benzidine exposure.

## **REFERENCES CITED**

ACGIH [1993]. 1993-1994 Threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

CFR. Code of Federal regulations. Washington, DC: U.S. Government Printing Office, Office of the Federal Register.

IARC [1972]. IARC monographs on the evaluation of carcinogenic risk of chemicals to man. Vol. 1. Lyon, France: World Health Organization, International Agency for Research on Cancer.

IARC [1982]. IARC monographs on the evaluation of carcinogenic risk of chemicals to humans. Vol. 29. Lyon, France: World Health Organization, International Agency for Research on Cancer.

NIOSH [1987a]. NIOSH guide to industrial respiratory protection. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 87-116.

NIOSH [1987b]. NIOSH respirator decision logic. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 87-108.

NIOSH [1992]. NIOSH recommendations for occupational safety and health: compendium of policy documents and statements. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 92-100.

NIOSH [1993]. Registry of toxic effects of chemical substances database: benzidine. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Division of Standards Development and Technology Transfer, Technical Information Branch.

OSHA [1990]. Method 65. OSHA analytical methods manual. Salt Lake City, UT: U.S. Department of Labor, Occupational Safety and Health Administration, OSHA Analytical Laboratory.

Proctor NH, Hughes JP, Fischman ML [1988]. Chemical hazards of the workplace. Philadelphia, PA: J.B. Lippincott Company.

