

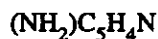
OCCUPATIONAL SAFETY AND HEALTH GUIDELINE FOR 2-AMINOPYRIDINE

INTRODUCTION

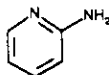
This guideline summarizes pertinent information about 2-aminopyridine for workers and employers as well as for physicians, industrial hygienists, and other occupational safety and health professionals who may need such information to conduct effective occupational safety and health programs. Recommendations may be superseded by new developments in these fields; readers are therefore advised to regard these recommendations as general guidelines and to determine periodically whether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

α -Aminopyridine; 1,2-dihydro-2-iminopyridine; 2-pyridylamine; o-aminopyridine; amino-2-pyridine; α -pyridinamine, 2 AP

• Identifiers

1. CAS No.: 504-29-0
2. RTECS No.: US1575000
3. DOT UN: 2671 55
4. DOT label: Poison

• Appearance and odor

2-Aminopyridine is a combustible, colorless or white, crystalline solid that has an odor described as "characteristic."

CHEMICAL AND PHYSICAL PROPERTIES

• Physical data

1. Molecular weight: 94.1
2. Boiling point (at 760 mm Hg): 210.6°C (411.1°F)
3. Specific gravity (water = 1): Greater than 1
4. Vapor density (air = 1 at boiling point of 2-aminopyridine): 3.2
5. Melting point: 58.1°C (136.6°F)
6. Vapor pressure at 25°C (77°F): 0.8 mm Hg
7. Solubility: Soluble in water, alcohol, benzene, ether, and acetone
8. Evaporation rate: Data not available

• Reactivity

1. Conditions contributing to instability: Heat, sparks, or open flame
2. Incompatibilities: Fires and explosions may result from contact of 2-aminopyridine with strong oxidizers, strong acids, or sodium nitrate.
3. Thermal decomposition products: Toxic gases (such as oxides of nitrogen, carbon dioxide, and carbon monoxide) may be released when 2-aminopyridine burns or is heated to decomposition.
4. Special precautions: None

• Flammability

The National Fire Protection Association has not assigned a flammability rating to 2-aminopyridine; other sources rate 2-aminopyridine as a moderate fire hazard.

1. Flash point: 68°C (154°F) (closed cup)
2. Autoignition temperature: Data not available
3. Flammable limits in air: Data not available

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4. Extinguishant: Use dry chemical, carbon dioxide, or alcohol foam to extinguish fires involving 2-aminopyridine. Do not use a solid stream of water because the stream will scatter and spread the fire. However, water spray may be used to cool fire-exposed containers.

Fires involving 2-aminopyridine should be fought upwind and from the maximum distance possible. Isolate the hazard area and deny access to unnecessary personnel. Emergency personnel should stay out of low areas and ventilate closed spaces before entering. Containers of 2-aminopyridine may explode in the heat of the fire and 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 (including a self-contained breathing apparatus) when fighting fires involving 2-aminopyridine. Chemical protective clothing that is specifically recommended for 2-aminopyridine may not provide thermal protection unless so stated by the clothing manufacturer. Firefighters' protective clothing may not provide protection against permeation by 2-aminopyridine.

EXPOSURE LIMITS

• OSHA PEL

The current Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) for 2-aminopyridine is 0.5 part per million (ppm) parts of air (2 mg/m^3) as an 8-hr time-weighted average (TWA) concentration [29 CFR 1910.1000, Table Z-1-A].

• NIOSH REL

The National Institute for Occupational Safety and Health (NIOSH) has established a recommended exposure limit (REL) of 0.5 ppm (2 mg/m^3) as an 8-hr TWA [NIOSH 1992].

• ACGIH TLV®

The American Conference of Governmental Industrial Hygienists (ACGIH) has assigned 2-aminopyridine a threshold limit value (TLV) of 0.5 ppm (2 mg/m^3) as a TWA for a normal 8-hr workday and a 40-hr workweek [ACGIH 1991b].

• Rationale for limits

The limits are based on the risk of systemic poisoning associated with exposure to 2-aminopyridine.

HEALTH HAZARD INFORMATION

• Routes of exposure

Exposure to 2-aminopyridine can occur through inhalation, ingestion, eye or skin contact, and absorption through the skin.

• Summary of toxicology

1. *Effects on Animals:* 2-Aminopyridine is a dermally absorbed, central nervous system stimulant and convulsant in animals. When instilled into the eyes of rabbits, 2-aminopyridine causes only mild, reversible injury [Grant 1986]. 2-Aminopyridine is rapidly absorbed through the skin and has caused convulsions and death in guinea pigs exposed by this route [Clayton and Clayton 1981]. The acute dermal LD_{50} in guinea pigs is 0.5 ml/kg (approximately 500 mg/kg) [Clayton and Clayton 1981]. The acute oral LD_{50} is 50 mg/kg in mice and 200 mg/kg in rats. Acutely poisoned animals exhibit tremors, excitement, seizures, and tetany before death from respiratory failure [Clayton and Clayton 1981]. 2-Aminopyridine is nonmutagenic in *Salmonella typhimurium* [NLM 1992].

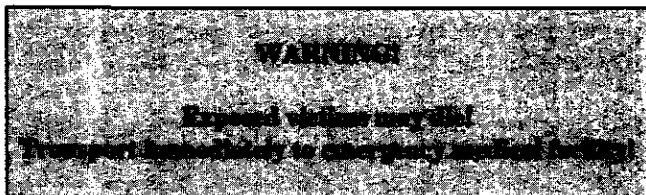
2. *Effects on Humans:* Intoxication from 2-aminopyridine can occur from inhalation of the dust or vapor or from skin absorption following direct contact. 2-Aminopyridine is a convulsant in humans and is moderately irritating to the skin and eyes [Clayton and Clayton 1981]. The lowest concentration and duration of exposure reported to be toxic in humans is 5 ppm for 5 hr; the toxic effects caused by this exposure include confusion and convulsions [NIOSH 1991]. A worker who was milling 2-aminopyridine developed high blood pressure, headache, nausea, and flushing of the extremities; subsequent air sampling demonstrated a level of 5.2 ppm; this worker had recovered completely by the following day [Clayton and Clayton 1981]. A chemical operator who continued to work for 1½ hr in clothing contaminated with 2-aminopyridine developed headache, difficult breathing, dizziness, and convulsions and died from respiratory failure [Clayton and Clayton 1981]. He may also have absorbed this substance through his skin [ACGIH 1991a]. Ingestion of as little as 60 mg in adult humans has resulted in severe poisoning, which included such signs and symptoms as: profuse sweating, burning of throat, weakness, nausea, disorientation, dizziness, thirst, ocular paresthesias, psychoticlike behavior, tremors, dyspnea, and convulsions [NLM 1992].

• Signs and symptoms of exposure

1. *Acute exposure:* Acute exposure to 2-aminopyridine can cause irritation, headache, dizziness, nausea, flushing of the extremities, elevated blood pressure, weakness, difficult breathing, confusion, ocular paresthesias, seizures, and stupor. In severe poisoning, exposure to this substance may cause respiratory failure and death.

2. *Chronic exposure:* No signs or symptoms of chronic exposure to 2-aminopyridine have been reported.

- **Emergency procedures**



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:* Irritation may result! *Immediately* flush the eyes with large amounts of water for at least 15 min, occasionally lifting the upper and lower eyelids.

2. *Skin exposure:* 2-Aminopyridine can cause skin irritation and 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 respirable 2-aminopyridine is inhaled, move the victim to fresh air *immediately*. Have the victim blow his or her nose or use a soft tissue to swab particulates from the nostrils.

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

4. *Ingestion exposure:* Take the following steps if 2-aminopyridine or a solution containing it is ingested:

- Do *not* induce vomiting.

- Have the victim rinse the contaminated mouth cavity several times with a fluid such as water.

- 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 2-aminopyridine and may result in worker exposures to this substance:

- Manufacture of pharmaceuticals, especially antihistamines

- Manufacture of hair dyes and other dyes

- Use of 2-aminopyridine in chemical synthesis

The following methods are effective in controlling worker exposures to 2-aminopyridine, depending on the feasibility of implementation:

- Process enclosure

- Local exhaust ventilation

- General dilution ventilation

- Personal protective equipment

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, placement of workers in jobs that do not jeopardize their safety or health, 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 2-aminopyridine, 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. These should concentrate on the function and integrity of the central nervous and respiratory systems. Medical monitoring for respiratory disease should be conducted using the principles and methods recommended by the American Thoracic Society [ATS 1987].

A preplacement medical evaluation is recommended to assess an individual's suitability for employment at a specific job and to detect and assess medical conditions that may be aggravated or may result in increased risk when a worker is exposed to 2-aminopyridine at or below the prescribed exposure limit. The licensed health care professional should consider the probable frequency, intensity, and duration of exposure as well as the nature and degree of any applicable medical condition. Such conditions (which should not be regarded as absolute contraindications to job placement) include a history or findings consistent with seizure or other central nervous system disorders or chronic respiratory disease.

- **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 2-aminopyridine exposure. The interviews, examinations, and medical screening tests should focus on identifying the adverse effects of 2-aminopyridine on the central nervous and respiratory systems. 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 tissue or fluids to provide an index of exposure to a toxic substance or metabolite. No biological monitoring test acceptable for routine use has yet been developed for 2-aminopyridine.

- **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 job 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.

WORKPLACE MONITORING AND MEASUREMENT

A worker's exposure to airborne 2-aminopyridine is determined by using two Tenax-GC tubes in series (the first tube contains a single 35-mg section and the second tube contains a single 17-mg section; both sections are 35/60 mesh). Samples are collected at a maximum flow rate of 0.2 liter/min until a maximum air volume of 12 liters is collected. The sample is then analyzed by gas chromatography using a flame ionization detector. This method is included in the OSHA Computerized Information System [OSHA 1986]. NIOSH has a similar method for analyzing 2-aminopyridine (Method S158) in the *NIOSH Manual of Analytical Methods* [NIOSH 1984].

PERSONAL HYGIENE

Because 2-aminopyridine can be absorbed through the skin in lethal amounts, workers should immediately remove any contaminated clothing and wash thoroughly with soap and water any areas of the skin that have come in contact with this substance.

Clothing and shoes contaminated with 2-aminopyridine should be removed immediately and provisions should be made for safely removing this chemical from these articles. Persons laundering contaminated clothing should be informed about the hazardous properties of 2-aminopyridine, particularly its potential for being absorbed through the skin in lethal amounts.

A worker who handles 2-aminopyridine should thoroughly wash hands, forearms, and face with soap and water before eating, using tobacco products, or using toilet facilities.

Workers should not eat, drink, or use tobacco products in areas where 2-aminopyridine is handled, processed, or stored.

STORAGE

2-Aminopyridine should be stored in a cool, dry, well-ventilated area in tightly sealed containers that are labeled in accordance with OSHA's hazard communication standard [29 CFR 1910.1200]. All electrical service in storage areas should be of explosionproof design. Containers of

2-aminopyridine should be protected from physical damage and should be stored separately from oxidizing agents, strong acids, sodium nitrate, heat, sparks, and open flame. Because empty containers may contain 2-aminopyridine residues, they should be handled appropriately.

SPILLS AND LEAKS

In the event of a spill or leak involving 2-aminopyridine, persons not wearing protective equipment and clothing should be restricted from contaminated areas until cleanup is complete. The following steps should be undertaken following a spill or leak:

1. Do not touch the spilled material.
2. Notify safety personnel.
3. Remove all sources of heat and ignition.
4. Provide maximum explosionproof ventilation.
5. Use nonsparking tools during cleanup.
6. Carefully collect solid material and place it in a covered container for disposal.
7. To the extent feasible, avoid generating dust during cleanup.

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

2-Aminopyridine 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

Employers are not required by the emergency release notification provisions of the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [40 CFR 355.40] to notify the National Response Center of an accidental release of 2-aminopyridine; there is no reportable quantity for this substance.

• Community right-to-know requirements

Employers are not required by Section 313 of SARA to submit a Toxic Chemical Release Inventory Form (Form R) to EPA reporting the amount of 2-aminopyridine 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. Although 2-aminopyridine is not specifically listed as a hazardous waste under the Resource Conservation and Recovery Act (RCRA) [40 USC 6901 et seq.], EPA requires employers to treat waste as hazardous if it exhibits any of the characteristics discussed above.

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 2-aminopyridine 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, 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 informa-

tion on the selection and use of respirators and on 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 possibility of skin contact with 2-aminopyridine. Gloves, aprons, boots, and chemical-protective suits should be worn when workers are handling this substance. Chemical protective clothing should be selected on the basis of available performance data, manufacturers' recommendations, and evaluation of the clothing under actual conditions of use. No reports have been published on the resistance of various protective clothing materials to 2-aminopyridine permeation; however, butyl rubber has been tested against chemically similar materials (pyridines) and has demonstrated good-to-excellent resistance. Since specific test data are not available for 2-aminopyridine, the information provided here should be considered as a guideline only. If permeability data are not readily available, protective clothing manufacturers should be requested to provide information on the best chemical protective clothing for workers to wear when they are exposed to 2-aminopyridine.

If 2-aminopyridine is dissolved in water or an organic solvent, the permeation properties of both the solvent and the mixture must be considered when selecting personal protective equipment and clothing.

Safety glasses, goggles, or face shields should be worn during operations in which 2-aminopyridine might contact the eyes (e.g., through dust particles or splashes of solution). Eyewash fountains and emergency showers should be available within the immediate work area whenever the potential exists for eye or skin contact with 2-aminopyridine. Contact lenses should not be worn if the potential exists for 2-aminopyridine exposure.

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