

NIOSH ALERT

Preventing Asthma and Death from Diisocyanate Exposure

WARNING!

Workers exposed to diisocyanates may develop serious or fatal respiratory disease.

Employers should take the following steps to protect workers from diisocyanate exposure:

- Make workers aware of the serious health effects that may result from diisocyanate exposures.
- Make workers aware of any materials that may contain or be contaminated with diisocyanates.
- When feasible, substitute a less hazardous material for diisocyanates.
- If substitution is not possible, use engineering controls such as closed systems and ventilation to minimize exposures.
- Provide appropriate respiratory protection to workers exposed to diisocyanates.

Workers should take the following steps to protect themselves from diisocyanate exposure:

- Be aware that the highest diisocyanate concentrations may occur inside containment structures.

- Use appropriate respiratory protection when working with diisocyanates.
- Wash hands and face before eating, drinking, or smoking outside the work area.
- Shower and change into clean clothes before leaving the worksite.
- Participate in medical monitoring and examination programs, air monitoring programs, or training programs offered by your employer.

For additional information, see **NIOSH ALERT: Request for Assistance in Preventing Asthma and Death from Diisocyanate Exposure** [DHHS (NIOSH) Publication No. 96-111]. Single copies of the Alert are available free from the following:

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4676 Columbia Parkway
Cincinnati, OH 45226

Fax number: (513) 533-8573
Phone number: 1-800-35-NIOSH (1-800-356-4674)
E-mail: pubstaft@niosdt1.em.cdc.gov



U.S. Department of Health and Human Services
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Preventing Asthma and Death from Diisocyanate Exposure DHHS [Español \(Spanish\)](#)

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Workers exposed to diisocyanates may develop serious or fatal respiratory disease.

The National Institute for Occupational Safety and Health (NIOSH) requests assistance in preventing asthma, other respiratory disease, and death from diisocyanate exposure. This Alert summarizes seven case reports of disease and deaths following occupational exposure to diisocyanates. Information about preventing adverse health effects from exposure to diisocyanates is urgently needed by workers and employers, small businesses, physicians, and other health care providers.

NIOSH therefore requests that editors of trade journals, safety and health officials, labor union leaders, employers, educators, and diisocyanate suppliers and manufacturers bring this Alert to the attention of all workers at risk. Your assistance will help prevent asthma and other respiratory disease in the 280,000 U.S. workers potentially exposed to diisocyanates.

Background

Diisocyanates are a group of low-molecular-weight aromatic and aliphatic compounds. The most common of these are toluene diisocyanate (TDI), methylene bisphenyl isocyanate (MDI), and hexamethylene diisocyanate

(HDI). Appendix A lists commonly used synonyms for these three diisocyanates. They are widely used in the manufacture of flexible and rigid foams, fibers, coatings such as paints and varnishes, and elastomers. Diisocyanates are increasingly used in the automobile industry, autobody repair, and building insulation materials. In this report, diisocyanates as a group will be referred to as isocyanates.

The world production of isocyanates is estimated to be 3 billion pounds annually [Woods 1987], and 280,000 U.S. workers are potentially exposed [NIOSH 1983; Dunn and Bradstreet 1983].

The major route of occupational exposure to isocyanates is inhalation of the vapor or aerosol; exposure may also occur through skin contact during the handling of liquid isocyanates. Occupational exposure normally occurs during the production and use of isocyanates—particularly during the mixing and foaming processes in the polyurethane foam industry. Exposures to airborne isocyanates may also occur from the melting or burning of polyurethane foams during fire fighting.

Current Exposure Limits

Occupational exposure standards for isocyanates are based on respiratory irritation and sensitization and carcinogenesis. Only the exposure standards for TDI and MDI are outlined here.

OSHA

The current Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) for TDI is 0.02 part per million parts of air (0.02 ppm), or 0.14 milligram per cubic meter of air (0.14 mg/m³) as a ceiling limit [29 CFR* 1910.1000]. When updating its air contaminants standard in 1989, OSHA decreased this limit to 0.005 ppm (0.036 mg/m³) as an 8-hour time-weighted average (TWA) and 0.02 ppm (0.14 mg/m³) as a short-term exposure limit. However, this standard was rescinded by court order in 1992.

The OSHA PEL for MDI is 0.02 ppm (0.2 mg/m³) as a ceiling limit.

*Code of Federal Regulations. See CFR in references.

NIOSH

In two separate criteria documents, NIOSH has recommended that TDI exposure be limited to 0.005 ppm (0.036 mg/m³) as a TWA for up to a 10-hour workday during a 40-hour workweek, with a ceiling concentration of 0.02 ppm (0.14 mg/m³) for any 10-minute period [NIOSH 1973, 1978]. This NIOSH recommended exposure limit (REL) was intended to prevent acute and chronic irritation and sensitization of workers but not to prevent responses in workers who are already sensitized. Available data do not indicate a concentration at which TDI vapor fails to produce adverse reactions in sensitized persons. NIOSH further recognized the carcinogenic potential of TDI and its isomers and recommended that exposures be reduced to the lowest feasible concentrations [NIOSH 1989].

The NIOSH REL for MDI is 0.005 ppm (0.05 mg/m³) as a TWA and 0.02 ppm (0.2 mg/m³) as a ceiling limit.

ACGIH

The American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value (TLV) for TDI is 0.005 ppm (0.036 mg/m³) as an 8-hour TWA and 0.02 ppm (0.14 mg/m³) as a short-term exposure limit. The ACGIH TLV for MDI is 0.005 ppm (0.05 mg/m³) as a TWA [ACGIH 1995].

Health Effects of Isocyanates

Irritation

TDI and other isocyanates are powerful irritants to the mucous membranes of the eyes and gastrointestinal and respiratory tracts [Swensson et al. 1955; Upjohn Company 1970]. Direct skin contact with TDI can also cause marked inflammation [Fisher 1967]. Respiratory irritation may progress to a chemical bronchitis with severe bronchospasm [Williamson 1965].

Sensitization and Asthma

Isocyanates can also sensitize workers, making them subject to severe asthma attacks if they are exposed again—even at concentrations below the NIOSH REL [NIOSH 1973, 1978]. Death from severe asthma in sensitized subjects has been reported [Fabbri et al. 1988].

Hypersensitivity Pneumonitis

Sporadic cases of hypersensitivity pneumonitis (HP) have also been reported in workers exposed to isocyanates [Charles et al. 1976; Fink and Schlueter 1978; Selden et al. 1989]. Individuals with acute HP typically develop symptoms 4 to 6 hours after exposure.

Symptoms are often flu-like, with fever, muscle aches, and headaches. Symptoms may also include a dry cough, chest tightness, and difficult breathing. Individuals with chronic HP often experience progressively more difficult breathing, fatigue, and weight loss [Parker et al. 1992].

Cancer

Data from recent studies of animals show that cancer is associated with exposure to commercial-grade TDI (an 80:20 mixture of 2,4- and 2,6-TDI). The responses of both rats and mice treated with TDI meet the OSHA criteria for classifying a substance as a potential occupational carcinogen [29 CFR 1990.112]. NIOSH therefore recommends that occupational exposure to TDI and its isomers be minimized [NIOSH 1989].

The carcinogenic effects of TDI [Loeser 1983; NTP 1986] were also investigated by the International Agency for Research on Cancer (IARC) and the World Health Organization (WHO) [IARC 1986; WHO 1987]. IARC concluded that data were sufficient to show that TDI causes cancer in animals. WHO concluded that TDI should be treated as a potential human carcinogen.

Case Reports

The following case reports highlight examples of isocyanate-induced asthma, other respiratory disease, and death.

Case No. 1–Spray Painting (One Death)

A 37-year-old male, self-employed car painter was admitted to the hospital with asthma symptoms [Fabbri et al. 1988]. These symptoms had first developed 5 years earlier and were thought to be related to his occupation. He had been working in the same environment for more than 20 years.

The car painter was diagnosed with occupational asthma induced by isocyanates and advised to change his job or avoid the use of polyurethane paints. He nevertheless continued to work as a car painter and used medications such as bronchodilators, cromolyn, and steroids to treat his asthma.

Six years later, he was wearing a mask and spraying a car with 2-component polyurethane paint when he developed severe, prolonged asthma. Despite medication, he remained symptomatic—especially at night. He returned to work, sprayed the polyurethane paint again, and developed severe asthma requiring emergency treatment. He died in the ambulance enroute to the hospital. The manufacturer reported that the paint contained small amounts of TDI, and a chemical analysis confirmed the presence of TDI mixed with solvents.

Case No. 2–Highway Spill

Two police officers developed asthma-like illness after a single exposure to TDI in the immediate vicinity of a tank car that had overturned on the highway [Luo et al. 1990]. After briefly directing traffic at the accident scene, both officers received medical care for severe symptoms, including burning eyes, throat irritation, cough, chest tightness, and difficult breathing. Treatment included steroids and a bronchodilator.

Both police officers developed a chronic bronchospastic disorder after their relatively brief exposure to high concentrations of TDI. Though considerable

improvement has occurred in both cases, symptoms have persisted for more than 7 years.

Case No. 3–Spray Painting

Occupational asthma was reported in three workers in the paint shops of a large assembly plant [Seguin et al. 1987]. When coworkers were also examined, six additional workers showed symptoms of occupational asthma.

Of the nine affected workers (males aged 23 to 59), six had significantly reduced lung function after an inhalation test using the paint containing isocyanates. The duration of exposure to isocyanates in the paint shops ranged from 3 to 5 years.

The authors of this study reported a 12% prevalence rate for occupational asthma.

Case No. 4–Isocyanate Foam Operation (One Death)

A maintenance worker became ill after repairing an MDI foaming system at a plant that manufactured artificial plants with polyurethane foam bases [NIOSH 1994a]. The worker later suffered recurrent bouts of respiratory illness (diagnosed as isocyanate- induced HP).

After showing further respiratory symptoms associated with isocyanate exposure, the worker quit his job but continued to experience coughing and progressive loss of lung function. His illness was eventually complicated by productive cough, weakness, sweats, muscle aches, and shortness of breath. Ultimately, he died.

Worksite evaluations found detectable air concentrations of MDI and inadequate ventilation systems in the foaming areas. Vapors and aerosols were observed rising into the faces of employees working with the foam. Skin contact with the curing foam was also noted during the survey.

Case No. 5–Wood Products Manufacturing

Ten workers at an engineered wood products plant developed occupational asthma from exposure to MDI [NIOSH 1993]. The workers were employed 1 to 8 months at the plant before their diagnosis of occupational asthma. None of the 10 workers reported preexisting asthma.

Respiratory symptoms included chest tightness, wheezing, and coughing at night. Six workers reported a relationship between symptoms and work: they either reported improved symptoms while away from work or increased symptoms on their first day back at work. Eight workers showed declines in lung function over the workweek or over their period of employment, or they showed increased lung function after treatment with a bronchodilator. Eight workers showed bronchial sensitivity when tested (methacholine challenge).

All 10 workers reported respiratory symptoms when they were in areas where MDI was used. The physician who examined the 10 workers recommended that they be removed from areas with any potential exposure to MDI.

Case No. 6—Coal Mining

Coal miners at a longwall mine complained of illness after exposure to MDI-based polyurethane rock glues [NIOSH 1994b]. These miners had sprayed glues onto rock strata.

They were supplied with air-purifying respirators (organic vapor cartridges) and chemical-resistant gloves that were not routinely worn. The exposed miners reported respiratory difficulties, asthma, shortness of breath, dizziness, headache, sore throat, fatigue, and contact dermatitis. Company medical records contained nine reports of health problems attributed to rock glue exposure.

The inappropriate glue-spraying procedure used at this mine was eliminated by the Mine Safety and Health Administration (MSHA). The manufacturer's instructions specify that the glues are only to be injected for roof support and that workers are to wear supplied-air respirators—not air-purifying respirators. Air-purifying respirators are not recommended because rock

glues are eye irritants and have poor warning properties, and because cartridges for these respirators have no end-of-service indicators for MDI.

Case No. 7–Isocyanate Roofing Foam

Isocyanate exposure has also occurred at nonindustrial worksites such as public schools. The management of a large metropolitan school district contacted NIOSH for assistance after a university study documented asthma in 13 of approximately 85 staff members from a middle school [NIOSH 1994c]. The report further suggested that as many as 34 staff members might be asthmatic.

NIOSH investigators determined that large quantities of polyurethane foams and isocyanate coating materials had recently been applied to the school roof on several occasions. School staff members reported odors during roofing application, suggesting possible exposures to roofing materials that included isocyanates. Later air sampling during a test pour of the roofing materials at another location indicated the release of isocyanates during roofing and a potential for exposure.

Conclusion

The cases described here reveal the potentially serious nature of respiratory disease after exposures to isocyanates. The following recommendations are intended to reduce the potential for exposed workers to develop adverse health effects. Because NIOSH regards TDI as a potential occupational carcinogen, appropriate engineering controls[†] and work practices[‡] should be used to reduce worker exposures to the lowest feasible concentration.

[†]Engineering controls are hazard controls designed into equipment and workplaces.

[‡]Work practices are procedures followed by employers and workers to control hazards.

Recommendations

Product Substitution

When feasible, employers should substitute a less hazardous material for isocyanates.

Closed Systems and Ventilation

Engineering controls such as closed systems and ventilation should be the principal method for minimizing isocyanate exposure in the workplace. Exhaust ventilation systems should be designed to capture and contain vapors and particulates. Ventilation equipment should be checked for adequate performance at least every 3 months.

Worker Isolation

Areas containing isocyanates should be restricted to essential workers. If feasible, these workers should avoid direct contact with these chemicals by using automated equipment operated from a control booth or room with separate ventilation.

Protective Clothing and Equipment

When there is potential for isocyanate exposure, workers should be provided with and required to use appropriate personal protective clothing and equipment such as coveralls, footwear, chemical-resistant gloves and goggles, full faceshields, and suitable respiratory equipment.

Respiratory Protection

The use of respirators is the least preferred method of controlling worker exposures. Respirators should not be used as the primary control for routine operations, but NIOSH recognizes that they may be used during situations such as implementation of engineering controls, some short-duration maintenance procedures, and emergencies. Only the most protective respirators should be used for situations involving exposures to isocyanates that have poor warning properties, are potent sensitizers, or may be carcinogenic. These respirators include any self-contained breathing

apparatus with a full facepiece operated in a pressure-demand or other positive-pressure mode, and any supplied-air respirator with a full facepiece operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in a pressure-demand or other positive-pressure mode.

Any respiratory protection program must, at a minimum, meet the requirements of the OSHA respiratory protection standard [29 CFR 1910.134]. Respirators must be certified by NIOSH and MSHA according to 30 CFR or by NIOSH (effective July 19, 1995) according to 42 CFR 84. A complete respiratory protection program should include (1) regular training and medical evaluation of personnel, (2) fit testing, (3) periodic environmental monitoring, (4) periodic maintenance, inspection, and cleaning of equipment, (5) proper storage of equipment, and (6) written standard operating procedures governing the selection and use of respirators. The program should be evaluated regularly. The following publications contain additional information about selection, fit testing, use, storage, and cleaning of respiratory equipment:

NIOSH Guide to Industrial Respiratory Protection [NIOSH 1987a]

NIOSH Respiratory Decision Logic [NIOSH 1987b]

Worker and Employer Education

Worker education is vital to a good occupational safety and health program. OSHA requires that workers be informed about materials that may contain or be contaminated with isocyanates, and the nature of the potential hazard [29 CFR 1910.1200]. Employers must transmit this information through container labeling, material safety data sheets (MSDS), and worker training.

Exposure Monitoring

Each employer who manufactures, transports, packages, stores, or uses isocyanates or products containing isocyanates should determine whether the potential exists for worker exposure.

Decontamination and Waste Disposal

Procedures for decontamination, waste disposal, and transport should be established for isocyanate-contaminated materials or equipment.

Medical Monitoring

A medical monitoring program should be established for the early detection and prevention of the acute and chronic effects of exposure to isocyanates. The worker's physician should be given information about the adverse health effects of exposure to isocyanates and the worker's potential for exposure.

Surveillance and Disease Reporting

NIOSH encourages surveillance of occupational asthma by State health departments. To enhance the uniformity of reporting, NIOSH recommends reporting guidelines and an asthma surveillance case definition (see Appendix B). These guidelines and the case definition are recommended for public health surveillance of work-related asthma reported by physicians and other healthcare providers. As of 1996, four State health departments—California, Massachusetts, Michigan, and New Jersey—are actively engaged in occupational asthma surveillance activities.

Acknowledgments

The principal contributors to this Alert are Karl Musgrave; Chris Piacitelli; Gregory Kullman; Steve Berardinelli, Jr.; Al Dieffenbach; and John Parker. Please direct comments, questions, or requests for additional information to the following:

Director
Division of Respiratory Disease Studies
National Institute for Occupational Safety and Health
1095 Willowdale Road
Morgantown, WV 26505-2888

Telephone number: 1-304-285-5750 or 1-800-35-NIOSH (1-800-356-4674).

We greatly appreciate your assistance in protecting the lives of U.S. workers.

Linda Rosenstock, M.D., M.P.H.

Director, National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention

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Appendix A

Diisocyanate synonyms

TDI

- 2,4-Diisocyanato-1-methylbenzene
- 2,4-Diisocyanatotoluene
- 2,4-TDI
- 2,4-Tolylene diisocyanate
- 4-Methyl-phenylene diisocyanate
- Di-iso-cyanatoluene
- Isocyanic acid, 4-methyl-m-phenylene ester
- Isocyanic acid, methylphenylene ester
- m-tolylene diisocyanate
- Toluene-2,4-diisocyanate
- Toluene diisocyanate

MDI

- 1,1-Methylenebis(4-isocyanatobenzene)
- 4,4'-Diisocyanatodiphenylmethane
- 4,4'-Diphenylmethane diisocyanate

- 4,4'-Methylenebis(phenyl isocyanate)
- 4,4'-Methylenediphenyl diisocyanate
- Bis(1,4-isocyanatophenyl)methane
- Bis(4-isocyanatophenyl)methane
- Diphenylmethane 4,4'-diisocyanate
- Diphenylmethane diisocyanate
- Methylenebis(4-isocyanatobenzene)
- Methylenebis(4-phenylene isocyanate)
- Methylene bisphenyl isocyanate
- Methylene-di-p-phenylene isocyanate
- Methylene di(phenylene isocyanate)

HDI

- 1,6-Diisocyanatohexane
- 1,6-Hexamethylene diisocyanate
- 1,6-Hexanediol diisocyanate
- Hexamethylene-1,6-diisocyanate
- Hexamethylene diisocyanate
- HMDI (4,4' dicyclohexylmethane diisocyanate)
- Isocyanic acid, hexamethylene ester

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Appendix B

Surveillance Guidelines for State Health Departments: Occupational Asthma

Reporting Guidelines

State health departments should encourage providers to report all suspected or diagnosed cases of occupational asthma. These should include persons with:

- A physician diagnosis of asthma AND
- An association between symptoms of asthma and work.

State health departments should collect appropriate clinical, epidemiologic, and workplace information on reported cases to set priorities for workplace investigations.

Surveillance Case Definition

- A physician diagnosis of asthma*
- An association between symptoms of asthma and work[†] and any one of the following:
 1. Workplace exposure to an agent or process previously associated with occupational asthma§ OR
 2. Significant work-related changes in FEV1 or PEF_R
 3. Significant work-related changes in airways responsiveness as measured by nonspecific inhalation challenge
 4. Positive response to inhalation provocation testing with an agent to which patient is exposed at work. Inhalation provocation testing with workplace substances is potentially dangerous and should be performed by experienced personnel in a hospital setting where resuscitation facilities are available and where frequent observations can be made over sufficient time to monitor for delayed reactions.

*Asthma is a clinical syndrome characterized by increased responsiveness of the tracheobronchial tree to a variety of stimuli [ATS 1987]. Symptoms of asthma include episodic wheezing, chest tightness, and dyspnea, or recurrent attacks of “bronchitis” with cough, sputum production, and rhinitis [Chan-

Yeung and Lam 1986]. The primary physiologic manifestation of airways hyper-responsiveness is variable or reversible airflow obstruction, which may be demonstrated by significant changes in the forced expiratory volume in 1 second (FEV1) or peak expiratory flow rate (PEFR). Airflow changes can occur spontaneously, with treatment, with a precipitating exposure, or with diagnostic maneuvers such as nonspecific inhalation challenge.

†Patterns of association can vary. The following examples are patterns that may suggest an occupational etiology: symptoms of asthma develop after a worker starts a new job or after new materials are introduced on a job (a substantial period of time may elapse between initial exposure and development of symptoms); symptoms develop within minutes of specific activities or exposures at work; delayed symptoms occur several hours after exposure, during the evenings of workdays; symptoms occur less frequently or not at all on days away from work and on vacations; symptoms occur more frequently on returning to work. Work-related changes in medication requirements may have similar patterns, also suggesting an occupational etiology.

§Many agents and processes have been associated with occupational asthma [Chan-Yeung and Lam 1986, Salvaggio et al. 1986], and others continue to be recognized.

¶Changes in nonspecific bronchial hyperactivity can be measured by serial inhalation challenge testing with methacholine or histamine. Increased bronchial reactivity (manifested by reaction to lower concentrations or methacholine or histamine) following exposure and decreased bronchial reactivity after a period away from work are evidence of work-relatedness.

Reprinted from CDC [1990], p. 121.

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- Make workers aware of any materials that may contain or be contaminated with diisocyanates.
- When feasible, substitute a less hazardous material for diisocyanates.
- If substitution is not possible, use engineering controls such as closed systems and ventilation to minimize exposures.
- Provide appropriate respiratory protection to workers exposed to diisocyanates.

Workers should take the following steps to protect themselves from diisocyanate exposure:

- Be aware that the highest diisocyanate concentrations may occur inside containment structures.
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- Wash hands and face before eating, drinking, or smoking outside the work area.
- Shower and change into clean clothes before leaving the worksite.
- Participate in medical monitoring and examination programs, air monitoring programs, or training programs, offered by your employer.

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