

V. WORK PRACTICES

Exposure to TDI has caused irritation of the respiratory tract and reduced pulmonary function; this can progress to a condition resembling asthma or chronic bronchitis [32,43], which in some cases has been fatal [22]. These effects have been observed in sensitized individuals exposed at concentrations as low as 7 $\mu\text{g}/\text{cu m}$ [45], although respiratory effects have generally been reported in unsensitized workers only at concentrations of 140 $\mu\text{g}/\text{cu m}$ or higher [90]. Irritation of the respiratory tract has also been observed in individuals exposed to MDI [61,97,98] and HDI [42]. Exposure to TDI and other diisocyanates at high concentrations, eg, during accidental spills, is a major cause of sensitization [31,41,42,52], and there is evidence that massive exposures may produce effects on the CNS [71,73]. Diisocyanates are also skin irritants and sensitizers [105,141]; however, effects on the skin from these compounds do not appear to have been a major problem in industry [35]. Eye contact with liquid TDI and TDI vapor has produced irritation and watering of the eyes [2,9,120], and it is likely that direct eye contact with other diisocyanates would produce similar effects.

Diisocyanates encompassing a wide range of molecular weights and physical properties (see Table XI-1) are available for use in industry. The potentials of these compounds to irritate the respiratory tract, mucous membranes, eyes, and skin vary depending on the particular diisocyanate being considered. The potential for skin irritation and eye injury is generally higher for the lower molecular weight diisocyanates and the severity of these irritant responses is reduced with increasing molecular weight [1,2,142,143].

The potential respiratory hazards encountered during the use of diisocyanates in the workplace are related to their vapor pressures [1,2,142]. The lower molecular weight diisocyanates tend to be more readily volatilized into the workplace atmosphere than the higher molecular weight diisocyanates [1,2]. Figure XI-1 presents graphically the decrease in vapor pressure with increasing molecular weight for several diisocyanates. The lower molecular weight diisocyanates, such as HDI and TDI, when handled without special precautions, can release amounts of vapor sufficient to be extremely irritating to the respiratory tract of workers [2,142]. Higher molecular weight compounds such as NDI, IPDI, and MDI present a lesser vapor hazard when handled in well-ventilated areas at normal room temperatures, ie, less than approximately 40 C (104 F) for MDI [1,2,6,104,121,142]. Although the vapor pressures of the higher molecular weight diisocyanates are relatively low, they may generate vapor concentrations sufficient to cause respiratory and mucous membrane irritation if they are handled in poorly ventilated areas. Air exhaust hoods may be necessary under such conditions [121]. High molecular weight diisocyanates like MDI may also present significant vapor hazards when heated or used in exothermic production processes [1,2,6,8].

The physical state of the diisocyanate being handled will also affect the potential hazards encountered during its use. MDI and NDI, which are normally solid materials at room temperature, present less vapor inhalation or skin contact hazard as a result of splashes or spills than the lower molecular weight liquid diisocyanates do [1,2]. However, workers should be aware of the possibility of respiratory and mucous membrane irritation from the dusts of such compounds, and of contamination of their clothing with the powdered diisocyanates. Operations involving the use of such compounds, such as weighing, should be performed with equipment incorporating a barrier between the worker and the diisocyanate. Local exhaust ventilation may also be necessary. Clothing contaminated with solid diisocyanate should be decontaminated and laundered as soon as possible to prevent further exposure of the worker and to avoid contamination of other work areas. Spills involving these compounds should also be decontaminated and cleaned up as soon as possible.

The processes and operations in which diisocyanates are used will affect the severity of the hazard. Industrial processes involving evaporation from large surface areas or spraying operations may result in a greater potential vapor hazard than operations involving pouring-in-place or frothing techniques [6,8,104,121]. Special hazards may arise in spraying operations since the diisocyanate-containing aerosol cloud may drift to areas beyond the immediate spraying area.

Diisocyanates react with water to form carbon dioxide and water-insoluble polyureas [11]. The rate of reaction is very slow for TDI and MDI at temperatures below 50 C. As the temperature increases, the reaction between these compounds and water becomes more vigorous. TDI and MDI will also react with bases, such as sodium hydroxide, ammonia, primary and secondary amines, acids, and alcohols. This reaction may be violent, producing enough heat to increase the evolution of diisocyanate vapor and the generation of carbon dioxide. These reactions, like the reactions with water, may lead to dangerously increased pressure in closed containers [144]. Thus, containers of diisocyanates should be kept closed as much as possible to prevent water, atmospheric moisture, or other reactive compounds from entering and vapors or solids from escaping.

Diisocyanates should be transported or stored in sealed, intact containers. A "sealed container" is one that has been closed and kept closed to the extent that there is no release of diisocyanates. An "intact container" is one that has not deteriorated or been damaged to the extent that diisocyanates are released. Diisocyanates in sealed, intact containers should pose no threat of exposure to employees; therefore, it is not necessary to comply with required monitoring and medical surveillance requirements in operations involving such containers. If, however, containers are opened or broken so that diisocyanates may be released, then all provisions of the recommended standard should apply. Indoor storage areas should be dry, fireproofed (automatic sprinkler systems should be considered), and well ventilated; temperature extremes in these areas should be avoided [9,121]. The storage area should have a firm floor made of some nonabsorbent material [6]. If diisocyanates are accidentally frozen during storage or while in transit,

they may be thawed by storage in a warm area [121]. Extreme caution must be used if heat is applied, and a flame or similar localized heat source should never be used.

Diisocyanates are transported in drums, tank trucks, or tank cars. Containers should be properly labeled and shippers should be aware of precautions to be taken for transporting, loading, and unloading the particular container and type of diisocyanate being transported. Emergency measures to be taken in the event of an accident or some type of damage to the container or tank en route should also be worked out in advance by the shipper and the supplier or producer [9]. The Hazardous Materials Regulations as promulgated by the US Department of Transportation in 49 CFR Subchapter C should be adhered to where applicable.

Where bulk quantities of diisocyanates are handled, adequate ventilation should be provided and respiratory protective equipment should be readily available. Workers should wear chemical safety goggles when handling solid diisocyanates and chemical safety goggles with face shields when using liquid diisocyanates. Local exhaust ventilation should be employed when opening containers of diisocyanates [9]. Local exhaust ventilation should also be used when performing laboratory operations involving diisocyanates.

Since the flashpoints of most diisocyanates are high, the compounds are not flammable under normal circumstances, although they can burn if they are heated sufficiently. Because of the wide range of physical and chemical properties of diisocyanates (see Table XI-1), it is important to be aware of the potential fire hazard that may be associated with a particular diisocyanate in the industrial setting in which it is used or stored. Any diisocyanate involved in a fire may produce high concentrations of toxic vapors, and only trained and properly equipped personnel should be involved in firefighting. All nonessential personnel should be evacuated from the area during a fire. Suitable extinguishing media for fighting diisocyanate-supported fires are dry chemical powder, carbon dioxide, or foam. Water should be used only if large quantities are available, since the reaction between water and a hot diisocyanate may be vigorous. After the fire is out, the area should be inspected by properly protected personnel, and any suspected residues should be decontaminated before other workers are permitted to return to the area.

Contact with diisocyanates will cause plastic and rubber materials to become brittle after a short time. This could result in leaks from plastic or rubber hoses. Where a particular machine requires high-pressure lines or hoses for diisocyanates, these lines should be made of polytetrafluorethylene or equivalent with metal braiding on the outside. Neither TDI nor MDI is corrosive to metals at temperatures normally encountered in industrial operations [144].

Under normal working conditions, where engineering controls and work practices are adequate to keep diisocyanate concentrations below the recommended environmental limits, employees should wear coveralls (heavy cotton material is

recommended) and gloves made of either rubber or polyvinyl chloride [144]. If liquid diisocyanates may be present on the floors of work areas, rubbers or shoe coverings made of materials resistant to the penetration of diisocyanates should be worn over leather safety shoes. Rubbers that become contaminated with diisocyanates should be decontaminated or cut up and discarded.

If splashes or contact with aerosols of diisocyanates are likely to occur, employees should wear rubber or polyvinyl chloride gloves and aprons and rubber boots; appropriate respiratory equipment, as described in Table I-1, should be readily available. Where supplied-air respirators are used, the air supply must come from a source not contaminated with diisocyanates [145]. For all workers near spray gun operations (within approximately 10 feet), an air-supplied hood, impervious gloves (rubber or polyvinyl chloride), tightly buttoned coveralls, and rubber galoshes or boots are needed [146]. Workers without this equipment should not be permitted close enough to spraying operations performed outdoors to be exposed to diisocyanate vapors or particulates. A minimum of 50 feet is recommended. For indoor spraying operations, the safe distance for unprotected workers will depend on the type and efficiency of the ventilation provided [147,60] while ambient conditions, such as wind direction and velocity, will be important in determining a safe distance for outdoor operations [146].

Cup-type chemical safety goggles with face shields should be worn wherever there is danger of liquid diisocyanate coming in contact with the eyes. For continuous eye protection under normal conditions, spectacle-type safety glasses with 48-wire mesh sideshields may be used. Equipment for eye protection must be in accordance with the American National Standard for Occupational and Educational Eye and Face Protection, Z87.1-1968 [148], as specified in 29 CFR 1910.133.

Protective clothing that has become contaminated with a diisocyanate to an extent that may result in an excessive respiratory or skin contact hazard should be promptly removed. Before being reused, the clothing should be soaked in a decontaminating solution (eg, 90% water, 2% liquid detergent, 8% concentrated ammonia solution) and then laundered normally. Employers are responsible for ensuring that employees who launder clothing contaminated with diisocyanates are provided with adequate protective equipment and are aware of the hazards of these compounds and appropriate methods for handling them safely. If an outside laundering facility is used, the laundry employer must be advised of the hazards involved in handling clothing contaminated with diisocyanates and of the requirements to ensure that the laundry employees are not exposed to diisocyanates.

When leaks or spills of diisocyanates occur, only properly trained and equipped personnel wearing appropriate protective clothing should be permitted to remain in the area [9]. If major spills occur, air-supplied masks or self-contained breathing apparatus as described in Table I-1 must be used by workers in the area. Leaking containers should be removed to the outdoors or to an isolated, well-ventilated area before the contents are transferred to other suitable containers. Adequate

facilities for handling spills should be provided, including suitable floor drainage and readily accessible hoses, mops, buckets, and absorbent materials. Spills should be cleaned up promptly. The effectiveness of water as a cleansing agent is considerably improved by adding 1-5% of ammonia, and adding 10% isopropyl alcohol further improves it. Oil-absorbent materials such as vermiculite are also useful in cleaning spills. After use, such material should be shovelled into an open steel container, and the container should then be covered and removed to a safe disposal area away from the operating area. The mixture should be soaked with water containing ammonia and should stand for 24 hours in an open or partially open container. The container can then be closed and discarded [67,68].

Liquid diisocyanates should never be washed directly down the drain with water, because the solids that result may plug the sewer line. Any existing regulations pertaining to the discharge of such materials into sewer lines should be strictly adhered to. Since spills of diisocyanates may freeze during cold weather, water and ammonia will merely coat the solid material with insoluble urea, stopping further reactions. In cold weather, cleanup should be performed with a mixture of equal parts of isopropyl alcohol and ethylene glycol [9,68]. A supply of this mixture should be on hand and ready for immediate use in cold weather.

If a worker's skin becomes contaminated to the extent that there is an increased inhalation hazard or the possibility of prolonged skin contact with liquid or solid diisocyanates, it should immediately be washed thoroughly with soap and water or isopropanol. If water is initially used to flush the skin, any remaining diisocyanate should be neutralized and removed with isopropanol [9]. If diisocyanates are splashed into the eyes, the eyes should be flushed with copious amounts of clean water for at least 15 minutes. The affected employee should then receive medical evaluation from a health professional and obtain further treatment if necessary [67].

Because of the potential hazards of exposure to diisocyanates, the importance of good housekeeping should also be emphasized. Spills should be cleaned up promptly, and all equipment used in the exposure areas, such as buckets, weighing containers, and funnels, should be decontaminated and cleaned immediately after use. Smoking and the carrying of smoking supplies should be prohibited in areas where exposure to diisocyanates may occur, as should preparing, storing, dispensing (including vending machines), and consuming food and beverages. Employees exposed to diisocyanates should be encouraged to wash their hands before eating, drinking, or smoking, and before and after using toilet facilities. The US Department of Labor regulations concerning general sanitation in the workplace as specified in 29 CFR 1910.141 should be adhered to.

Employees should be instructed on the health hazards of diisocyanates and the precautions to be followed in handling them. They should be trained to report promptly to their supervisors all leaks, suspected failures of equipment, exposures to diisocyanates, or symptoms of exposure. The location of safety showers and eyewash fountains should be clearly marked, and appropriate warning signs and

labels should be prominently displayed in exposure areas and on containers of diisocyanates. Emergency exits should be provided and be accessible at all times. All emergency shower, eyewash, protective, and firefighting equipment should be checked periodically to ensure its serviceability.

VI. DEVELOPMENT OF STANDARD

Basis for Previous Standards

In 1959, the American Conference of Governmental Industrial Hygienists (ACGIH) adopted a Threshold Limit Value (TLV) for TDI of 0.1 ppm (0.7 mg/cu m) as an 8-hour TWA concentration limit [149]. According to Elkins et al [32], this value was first proposed by Ayscue in 1954 and was based on the results of animal experiments conducted at Du Pont's Haskell Laboratory. In 1957, Zapp [36] also recommended that this limit not be exceeded because respiratory irritation occurred in animals exposed to TDI at concentrations of 1-2 ppm. He noted that TDI and similar diisocyanates are strong irritants to the skin, eyes, and gastrointestinal and respiratory tracts and that they may cause asthma-like symptoms in workers.

In 1962, the ACGIH reduced the TLV for TDI to 0.02 ppm (0.14 mg/cu m) [150]. The 1962 Documentation of Threshold Limit Values cited the study of Elkins et al [32], who reported respiratory irritation and asthma-like symptoms in workers in several plants where TDI concentrations were considerably below 0.1 ppm. The 1962 documentation [151] cited a Threshold Limits Committee Report by Elkins that presented similar information. A threshold limit of 0.01-0.03 ppm was suggested to minimize the respiratory effects of TDI. The 1962 documentation [151] concluded that a TLV of 0.02 ppm (0.14 mg/cu m) was necessary to protect against allergic sensitization.

In 1963, the ACGIH [152] noted that a TLV in the form of a TWA concentration limit might not provide a sufficient safety factor for fast-acting substances. Consequently, the TLV for TDI, which remained at 0.02 ppm (0.14 mg/cu m), was changed to a ceiling value that should not be exceeded.

Subsequent editions of the Documentation of Threshold Limit Values in 1966 [153] and 1971 [154] contained several additional reports of the effects of TDI on experimental animals. The 1971 documentation also cited studies by Williamson [41], which reported that workers were affected by TDI at concentrations normally below 0.02 ppm. The data of Peters et al [84,85], suggesting pulmonary function changes in workers exposed to concentrations of TDI below 0.01 ppm, were reported, but these changes were not considered of sufficient importance to invalidate the existing limit. A TLV of 0.02 ppm (0.14 mg/cu m) was considered "sufficiently low to prevent substantially all sensitization and to minimize allergic attacks."

For MDI, the ACGIH adopted a TLV of 0.02 ppm (0.2 mg/cu m) in 1965 [155]. This limit was intended as a ceiling value not to be exceeded. The 1971 Documentation of Threshold Limit Values [154] described the basis for this limit. Although the vapor pressure of MDI is relatively low, the 1971 documentation [154] noted that significant vapor concentrations occurred in the workplace.

Isocyanates in general were reported to irritate the skin, eyes, and respiratory tract and to cause respiratory sensitization when sufficient vapor concentrations were present even for a short time [120]. Konzen et al [60] observed an immunologic response in workers exposed to MDI at approximately 1.3 ppm-minute but not in workers exposed at 0.9 ppm-minute. Bruckner et al [52] noted that workers might become sensitized to isocyanates when exposed at concentrations above 0.02 ppm. According to the 1971 documentation [154], available data indicated that MDI was similar to TDI in its irritant and sensitizing properties, suggesting that a similar ceiling value of 0.02 ppm (0.2 mg/cu m) was warranted.

In the United States, occupational exposure standards for diisocyanates have been established only for TDI and MDI. According to the International Labour Office [156], occupational exposure limits for TDI, MDI, and several other diisocyanates have been set by foreign countries. These limits are summarized in Tables VI-1 and VI-2.

Current Federal standards (29 CFR 1910.1000) for the diisocyanates are ceiling limits of 0.02 ppm (0.14 mg/cu m) for TDI and 0.02 ppm (0.2 mg/cu m) for MDI.

In 1973, NIOSH [37] published criteria for a recommended standard for occupational exposure to TDI, recommending a TWA limit of 0.005 ppm (0.036 mg/cu m) and a ceiling limit of 0.02 ppm (0.14 mg/cu m). A careful review of the data of Elkins et al [32] revealed cases of respiratory illness in plants where average TDI concentrations were below 10 ppb (70 µg/cu m) but none in plants where concentrations were below 7 ppb (50 µg/cu m). A TWA limit of 5 ppb (36 µg/cu m) was therefore considered to provide some margin of safety. A ceiling limit of 20 ppb (140 mg/cu m) was based primarily on the findings of Hama [79], who reported that workers had no symptoms at concentrations below 10 ppb but developed respiratory illness within 1 week when concentrations rose to 30-70 ppb; when concentrations were reduced to 10-30 ppb, there were no further complaints. The recommended ceiling was intended to protect against irritative effects of TDI in nonsensitized workers, but evidence was insufficient to determine whether it would also protect against sensitization. The document noted that no evidence was available to point to a concentration of TDI that would be safe for workers already sensitized to TDI. The present document reexamines the earlier recommendations for a TDI standard, taking into account more recent information that has become available since 1973.

Basis for the Recommended Standard

(a) Permissible Exposure Limits

The available data indicate that at least three types of effects, direct irritation, sensitization, and chronic decrease in pulmonary function, should be

TABLE VI-1
OCCUPATIONAL EXPOSURE LIMITS (MG/CU M) FOR TDI AND MDI

Country	TDI	MDI
United States	0.14*	0.2*
Australia	0.14*	0.2*
Belgium	0.12	0.2
Czechoslovakia	0.07** 0.14*	- -
Federal Republic of Germany	0.14***	0.2***
Finland	0.14*	0.2*
German Democratic Republic	0.1** 0.1 (STEL)*	0.15** 0.15*
Hungary	0.5	-
Italy	0.5	0.7
Japan	0.14	-
Netherlands	0.14	0.2*
Poland	-	0.1*
Rumania	0.1** 0.3	0.15* -
Sweden	0.07	0.1* ***
Switzerland	0.14*	0.2* ***
USSR	0.5*	-
Yugoslavia	0.14	0.2

*Ceiling limit

**TWA

***Designated as a sensitizer

Adapted from reference 156

TABLE VI-2
OCCUPATIONAL EXPOSURE LIMITS (MG/CU M) FOR OTHER DIISOCYANATES

Compound	Country	Limit
Hexamethylene diisocyanate (HDI)	Bulgaria	0.05*
	Federal Republic of Germany	0.14**
	German Democratic Republic	0.05*
	Poland	0.05
	Rumania	1***
	Switzerland	0.14**
	USSR	0.05****
Yugoslavia	0.05	
Isophorone diisocyanate (IPDI)	Belgium	****
	Federal Republic of Germany	0.18**
	Netherlands	****
	Switzerland	0.18***
Methylene-bis (4-cyclohexyl isocyanate)	Belgium	0.11*
	Netherlands	0.11
	Switzerland	0.22**
1,5-Naphthylene Diisocyanate (NDI)	Federal Republic of Germany	0.18**

*Ceiling limit

**Designated as a sensitizer

***TWA concentration

****"Skin" notation

Adapted from reference 156

considered in establishing an exposure limit for the diisocyanates. At relatively high concentrations, the diisocyanates produce direct irritation of the respiratory tract; such irritation has frequently been reported in workers exposed to spills or other sources of high concentrations [31,40,74,80,93], but there are few data to indicate a threshold concentration for this effect. In experimental 10-minute exposures, all of six volunteers experienced nose and throat irritation at 3,600 $\mu\text{g}/\text{cu m}$, one of six at 710 $\mu\text{g}/\text{cu m}$, and none at 360 $\mu\text{g}/\text{cu m}$; none of the volunteers reported chest symptoms from these brief exposures [38]. At an automobile plant, all 12 workers exposed to TDI developed severe respiratory symptoms during 1 week when concentrations rose to 210-500 $\mu\text{g}/\text{cu m}$, but they had no symptoms when concentrations remained below 210 $\mu\text{g}/\text{cu m}$ [79]. The latter study was the primary basis for the ceiling limit of 20 ppb (140 $\mu\text{g}/\text{cu m}$) for TDI recommended by NIOSH in 1973 [37]. Since no reports have been found of irritative effects in workers exposed below this level, this appears to indicate that this ceiling limit provides adequate protection for unsensitized workers.

In individuals who are sensitized to diisocyanates, exposure at concentrations well below this limit can produce symptoms of asthma. Several reports [43,45-47,57] have described reactions in sensitized workers exposed to TDI at 35 $\mu\text{g}/\text{cu m}$ or less. Sensitization to diisocyanates may involve an immunologic mechanism [62] and pharmacologic hyperreactivity to bronchoconstrictors [63,66]; either or both types of response may be present in an individual showing sensitivity to diisocyanates [46,47,56]. No threshold concentration for such reactions has been identified, but there is evidence that, for some individuals, it may be unmeasurably low [31,52,56]; thus, it is not possible at this time to establish a level below which sensitized workers will not experience adverse respiratory effects from exposure to diisocyanates.

Several studies have shown that 5-20% of the workforce may become sensitized to diisocyanates [32,52,56,83]. There is evidence, however, that the incidence of sensitization can be reduced by controlling exposures. The data of Elkins et al [32] on 15 TDI plants showed that all plants where average exposures exceeded 70 $\mu\text{g}/\text{cu m}$ had workers with TDI-related respiratory illness, but no such illnesses were reported in plants where average exposures were 50 $\mu\text{g}/\text{cu m}$ or lower. On the other hand, Weill [57] reported instances of sensitization developing in a plant where average TDI exposures ranged from 14 to 50 $\mu\text{g}/\text{cu m}$. These studies did not report the frequency or magnitude of excursions above these averages, so that the more precise estimates of exposure concentrations cannot be determined.

Several reports [31,41,42,52] have indicated that sensitization may follow exposure to spills or other unusually high concentrations. However, Pepys et al [43] described sensitization, verified by challenge testing with TDI, in four workers who had no known exposure to spills. Similar sensitization was reported by Carroll et al [45] in four office workers employed in building adjacent to a TDI factory. Two NIOSH health hazard evaluations [93,95] reported that, where TDI concentrations were 7 $\mu\text{g}/\text{cu m}$ or below, only workers previously sensitized at

higher concentrations had respiratory symptoms. The indication of a dose-response effect in sensitized individuals [45,54,57] suggests that the number of already sensitized individuals who develop an overt asthmatic reaction can also be reduced by lowering exposure levels.

Exposure to diisocyanates may also cause chronic respiratory effects measurable as long-term decrement in pulmonary function, especially FEV₁, in excess of that expected from aging. It is not clear from existing data whether this change occurs only in sensitized workers or whether it may also affect workers who show no clinical symptoms from diisocyanate exposure. The findings of Porter et al [56] indicate that some workers who are sensitive to TDI and who have anti-TDI antibodies may exhibit normal pulmonary function, while others with clinical symptoms of sensitization but negative results on immunologic tests may have severely impaired pulmonary function. In the study conducted by Wegman et al [90], in which workers exposed at concentrations above 20 µg/cu m had a significantly greater decrease in FEV₁ than those exposed at lower concentrations, the workforce studied included both sensitized and unsensitized individuals. In the plant studied by Weill and colleagues [57-59], where workers who showed symptoms of clinical sensitization were not included in the study population, the investigators found no significant effects on lung function related to TDI exposures at average concentrations of 14-50 µg/cu m. These findings indicate that the TWA limit of 5 ppb (35 µg/cu m) for TDI recommended by NIOSH in 1973 [37], which was based on the findings of Elkins et al [32], provides adequate protection against chronic effects of TDI on pulmonary function of workers who are not sensitized.

Environmental data for the other diisocyanates are insufficient to establish a safe exposure limit. The diisocyanates commonly used in industry are respiratory irritants [2]. In a plant where area samples showed MDI concentrations of 10-150 µg/cu m and breathing zone concentrations for 6 sprayers were 120-270 µg/cu m, 34 of 35 workers had eye, nose, or throat irritation, and nearly half had wheezing, shortness of breath, and chest tightness [96]. In another plant, 3 of 29 workers exposed to MDI at 50-110 µg/cu m had respiratory symptoms [61]. Nine of 18 workers exposed to HDI at less than 300 µg/cu m and to an HDI trimer at less than 3,800 µg/cu m had irritation of the upper respiratory tract, cough, or chest tightness [100].

Like TDI, other diisocyanates are likely to be reactive with biologic macromolecules, such as proteins, and thus are potential sensitizers. Some authors [60,61] have reported that MDI produces respiratory sensitization, since affected workers gave positive results in immunologic tests. The assumption of a common mechanism of action suggests that structurally similar diisocyanates might produce cross-sensitization; there is one report [53] of positive tests for antibodies against MDI in workers sensitized to TDI, but the validity of these results is questionable because of the lack of characterization of the test antigen used. A study of skin sensitization [69] suggested that workers exposed to TDI and MDI were cross-sensitized to IPDI. In another study [47], some workers with previous exposure only to TDI had bronchial reactions to MDI and HDI as well. These workers were

significantly more hyperreactive to histamine than workers who reacted to TDI only, suggesting that cross-reactivity might involve a nonspecific pharmacologic mechanism.

The predicted reactivity of the diisocyanates with biologic macromolecules is the probable basis for their immunologic effects and perhaps for the respiratory symptoms and effects on pulmonary function produced at low concentrations. It is therefore reasonable to expect that other diisocyanates react similarly to TDI on a molar basis.

None of the studies completed since 1973 provides a clear indication that unsensitized workers suffer adverse effects from exposure to TDI at concentrations below the limits that were recommended by NIOSH, 20 ppb (140 µg/cu m) as a ceiling concentration and 5 ppb (35 µg/cu m) as a TWA concentration [37]. The report of Wegman et al [90] that workers exposed to TDI at concentrations above 25 µg/cu m showed an excessive long-term decrement in pulmonary function does not provide adequate justification to change these limits; it contains insufficient information on individual changes in pulmonary function, the effect of sensitization on these measurements, and the possible role of other chemicals. Another report [93] of respiratory effects in workers whose average exposure was reportedly below 35 µg/cu m did not provide sufficient information to indicate whether some of these workers might have been sensitive to TDI, and, if so, whether they might have become sensitized at concentrations in excess of the recommended ceiling limit.

In the absence of data indicating that any of the diisocyanates is substantially less toxic than TDI, the exposure concentrations recommended in 1973 should be extended to all diisocyanates. It is recommended that exposure to the diisocyanates be controlled so that no employee is exposed at concentrations in excess of the following environmental limits, equivalent, in the case of volatile diisocyanates that occur as vapors, to a TWA limit of 5 ppb for a 10-hour workshift, 40-hour workweek, and a ceiling limit of 20 ppb for a 10-minute sampling period:

	<u>TWA</u>	<u>Ceiling</u>
Toluene diisocyanate (TDI)	35 µg/cu m	140 µg/cu m
Diphenylmethane diisocyanate (MDI)	50 µg/cu m	200 µg/cu m
Hexamethylene diisocyanate (HDI)	35 µg/cu m	140 µg/cu m
Napthalene diisocyanate (NDI)	40 µg/cu m	170 µg/cu m
Isophorone diisocyanate (IPDI)	45 µg/cu m	180 µg/cu m
Dicyclohexylmethane 4,4'-diisocyanate (hydrogenated MDI)	55 µg/cu m	210 µg/cu m

If other diisocyanates are used, employers should observe environmental limits equivalent to a ceiling concentration of 20 ppb and a TWA concentration of 5 ppb.

(b) Sampling and Analysis

The method recommended for sampling and analysis of diisocyanates is capable of detecting TDI, MDI, and HDI at concentrations as low as 2-5 $\mu\text{g}/\text{cu m}$ [123]. Because of this sensitivity, the recommended sampling time has been shortened to 10 minutes, rather than the 20-minute sampling period required for the Marcali method recommended in the 1973 TDI document [37]; this permits more accurate determinations of peak exposures.

The recommended method also permits separation of different diisocyanates in the same sample. It has not been tested with diisocyanates other than TDI, MDI, and HDI, but, with appropriate modifications and solvent systems, it should be capable of detecting these compounds in the same range.

The recommended method for sampling airborne diisocyanates consists of drawing air at a rate of 2 liters/minute for 10 minutes through two serially connected all-glass midjet impingers, each containing 15 ml of absorbing solution. The use of two impingers in series is necessary until a reproducible collection efficiency is established for any given operation, since absorber collection efficiency is highly variable [44,111,116,125,137]. The diisocyanates react with the absorbing solution to form specific urea derivatives which are then injected into the high-speed liquid chromatograph for analysis. The method is described in detail in Appendix I.

(c) Medical Surveillance and Recordkeeping

Respiratory effects from exposure to diisocyanates have included chronic bronchitis [20,21], asthmatic reactions [43,45] and decreased pulmonary function [81,87]. To prevent development of serious respiratory symptoms, a medical surveillance program should provide for the timely detection of adverse health effects that develop from exposure to diisocyanates.

Employees with a history of respiratory illness, especially asthma, and those exposed to other respiratory irritants, eg, smokers, may be at increased risk of developing adverse health effects from exposure to diisocyanates, and they should be counseled on this risk. All employees should be monitored so that work-related symptoms or loss of pulmonary function can be detected early. Employees who develop symptoms of TDI sensitization should be counseled on the risks of continuing to work with TDI.

Each employee should receive a thorough preplacement medical examination, which includes a history of exposure to diisocyanates, a smoking history, and a history of respiratory illnesses. Each employee should receive pulmonary function tests, including FEV 1 and FVC, and a chest X-ray before beginning work in any

plant manufacturing or using diisocyanates. For employees with occupational exposure to diisocyanates, physical examinations should be repeated at least annually. Because of seasonal and diurnal variations in pulmonary function, the periodic examination of an individual employee should be performed at about the same time each year and at the same time of day, so that changes in respiratory function can be evaluated. Chest X-rays are not required at periodic examinations, and should be repeated at the discretion of the examining physician. Records of medical examinations should be kept for at least 30 years after the employee's last exposure to diisocyanates.

The previous NIOSH criteria document on TDI [37] recommended a leukocyte count with differential as part of the preplacement medical examination and suggested periodic eosinophil counts. However, there is no evidence at this time that blood findings are a significant indicator of adverse effects of TDI exposure. This change in the recommendations for the medical examination is consistent with the failure to find eosinophils in TDI-sensitized individuals in recent studies [43,54,58].

(d) Personal Protective Equipment and Clothing

Where engineering controls are used to keep diisocyanate concentrations at or below the recommended exposure limits, minimal protective clothing is needed to safeguard workers. Under these conditions workers should wear coveralls and rubber or polyvinyl chloride gloves [144]. Where liquid diisocyanates may be present on floors, protective shoe coverings should be worn.

If the potential exists for splashes or contact with aerosols of diisocyanates, employees should be provided with face shields (20-cm minimum) with goggles, rubber or polyvinyl chloride gloves and aprons, rubber boots, and appropriate respiratory equipment as described in Table I-1. Because diisocyanates have poor warning properties [36,39], the use of chemical cartridge respirators or gas masks is not recommended. At present, air-purifying respirators with an end-of-service-life indicator are not available for the diisocyanates. Demand-type (negative pressure) supplied-air respirators are not recommended because of the possibility of facepiece leakage. Workers within 10 feet of a unit spraying material containing diisocyanates should wear full-body protective clothing and appropriate respiratory protective devices [60,147].

All protective clothing that becomes contaminated with diisocyanates should be replaced or thoroughly decontaminated in a solution of 8% ammonia and 2% liquid detergent in water and cleaned before reuse. Lockers should be provided for workers so that work and street clothes can be stored separately. The employer should arrange for laundering of all work clothes and ensure that laundry workers are aware of the hazards of exposure and appropriate safety precautions.

(e) Informing Employees of Hazards

At the beginning of employment, all employees should be informed of the hazards from exposure to diisocyanates. Brochures and pamphlets may be effective aids in informing employees of hazards. In addition, signs warning of the danger of exposure to diisocyanates should be posted in any area where occupational exposure to the diisocyanates is likely. Access to areas of potential high exposure should be restricted to employees equipped with appropriate protective gear. A continuing education program, which includes training in the use of protective equipment such as respirators and information about the value of the periodic medical examinations, should be available to the employees. Employees exposed to diisocyanates should be informed that symptoms of exposure, such as nocturnal dyspnea, may occur several hours after the end of the workshift. Because of the possibility of sensitization to the diisocyanates, employees should be warned that the improper home use of polyurethane products, such as foam kits and varnishes, that contain diisocyanates may increase their risk of developing work-related health problems. Employees should be instructed in their own responsibility for following work practices and sanitation procedures to help protect the health and provide for the safety of themselves and their fellow employees.

(f) Engineering Controls and Work Practices

There is evidence that workers can become sensitized to diisocyanates during brief exposures at high concentrations [42,93]. Effective engineering controls and good work practices must be emphasized to minimize the possibility of such exposures.

Engineering controls, such as process enclosure or local exhaust ventilation, should be used where needed to maintain environmental concentrations of diisocyanates at or below the recommended limits. These systems should be designed to prevent the accumulation or recirculation of diisocyanates in the workplace environment and to effectively remove diisocyanate vapors or aerosols from the breathing zone of the employees. The ventilation systems should be periodically checked, including airflow measurements, to ensure that the systems are working properly. Exhaust ventilation systems discharging to outside air must conform to applicable local, state, and Federal air pollution regulations and must not constitute a hazard to employees or to the general public.

Diisocyanates should be protected from extreme heat or direct sunlight. Because of the reactivity of diisocyanates with water, caution should be taken to prevent moisture from entering containers. Diisocyanates should not be stored near acids, bases, alcohols, or amines. Containers of diisocyanates should be periodically inspected to assure that they are tightly sealed and that the integrity of the containers is maintained. Leaking containers should be removed to the outdoors or to an isolated, well-ventilated area before the contents are transferred to other suitable containers [144].

The flashpoints of most diisocyanates are high, and the compounds will not burn under normal circumstances, although they will burn if heated sufficiently. The combustion of diisocyanates produces high concentrations of toxic fumes, and appropriate protective equipment should be worn by firefighters. For fighting diisocyanate-supported fires, dry chemical powder, carbon dioxide, or foam extinguishing media should be used. Water should only be used if large quantities are available [144]. Only essential personnel should be permitted in the area during the actual firefighting, and unprotected workers should not be permitted back into the area until it has been thoroughly inspected and any suspected diisocyanate residues have been decontaminated.

Good housekeeping in the workplace is of prime importance in reducing exposure to diisocyanates. Adequate facilities for handling spills and leaks of diisocyanates should be provided, and workers should be thoroughly trained in cleanup procedures. Spills should be promptly cleaned up, and all equipment used in the exposure areas, such as buckets, weighing containers, and funnels, should be decontaminated and cleaned immediately after use. To reduce the possibility of leaks, plastic or rubber hoses, which become brittle from contact with diisocyanates, should be checked and replaced regularly.

Storing, handling, dispensing, and consuming food should be prohibited in work areas, regardless of the concentrations of diisocyanates. In addition, it is recommended that employees who work in areas that use diisocyanates wash their hands thoroughly before eating or using toilet facilities. Smoking should not be permitted in areas where diisocyanates are stored or used because of the possibility that smoking materials may become contaminated with diisocyanates.

(g) Monitoring and Recordkeeping Requirements

In addition to a program of regular personal monitoring of air concentrations, continuous area monitoring is strongly recommended where aliphatic diisocyanates such as TDI and MDI are present. This will permit engineering controls to be modified or improved to keep the concentrations of diisocyanates at or below the recommended limits. Monitoring should also be performed whenever there is a change in the process or materials used that could increase the exposure of employees.

Employers should monitor exposure of employees to diisocyanates by taking a sufficient number of breathing-zone samples to adequately characterize exposures for every operation. In determining the sampling strategy for a particular worker, the process and the job description of the worker should be considered, and those process cycles in which potential exposure is greatest should be given prime consideration.

Records should be kept for all sampling operations and should include the type of personal protective devices in use, if any, and the sampling and analytical methods used. Employees or their designated representatives should have access to

records of their own environmental exposures. These records should be kept at least 30 years after the employee's last exposure to diisocyanates.