Isocyanates

Navy and Marine Corps Public Health Center
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1. References

a. What are Aliphatic Diisocyanates? American Chemistry Council. 2019.

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l. Occupational Safety and Health Administration (OSHA). 29 CFR 1910.94. Occupational Health and Environmental Control. Ventilation.

m. Occupational Safety and Health Administration (OSHA). 29 CFR 1910.134. Respiratory Protection.

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2. What are Isocyanates?

Isocyanates are chemicals that contain at least one isocyanate group in their structure. An isocyanate group consists of one nitrogen, one carbon, and one oxygen connected by double bonds (N=C=O), and attached to the parent molecule by the nitrogen atom. If the group is attached by the oxygen, it is a cyanate. Diisocyanates (monomers) are chemicals containing two isocyanate functional groups. Some common examples of monomeric isocyanates include 1,6-hexamethylene diisocyanate (HDI); 2,4- and/or 2,6-toluene diisocyanate (TDI); isophorone diisocyanate (IPDI); isophorone diisocyanate (IPDI); 4,4` diphenylmethane diisocyanate (MDI); and methylene bis (4-cyclohexylisocyanate) (HMDI).

Figure 1. 1,6-Hexamethylene Diisocyanate (HDI)

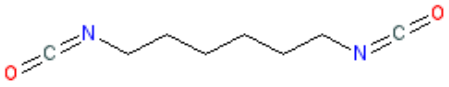


Figure 2. 2,6-Toluene Diisocyanate (TDI)

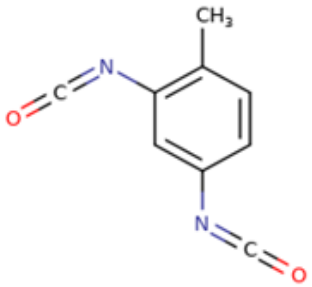


Figure 3. Isophorone Diisocyanate (IPDI)

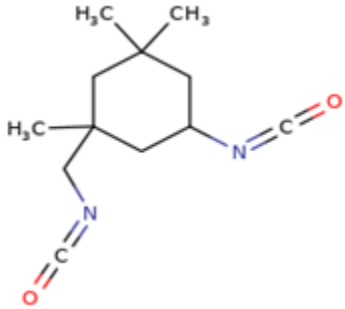
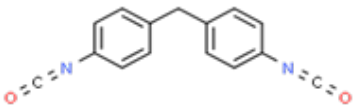


Figure 4. Methylene Diphenyl Diisocyanate (MDI)



These isocyanates can be classified into two subgroups: aromatic diisocyanates and aliphatic diisocyanates.

Aromatic diisocyanates include TDI and MDI. TDI is used primarily in the production of flexible foams. MDI is used in the production of a variety of polyurethane products such as elastomers, sealants, adhesives and coatings. Aromatic diisocyanates are more reactive than aliphatic diisocyanates. When exposed to UV light, aromatic diisocyanates oxidize more easily than aliphatic diisocyanates (Reference a).

Aliphatic diisocyanates include HDI, methylene dicyclohexyl diisocyanates or hydrogenated MDI (HMDI), and IPDI. They are used primarily to make resin used in paints and surface coating applied in the adhesive, automotive, marine and aircraft industries. The paints and surface coating with aliphatic diisocyanates have excellent resistance to chemicals, abrasion, and have weather resistant characteristics which includes gloss retention and resistance to yellowing and chalking (Reference a).

The diisocyanate monomers (single unit) can react with one another and various other chemicals to form larger molecules, from dimers and trimers (two and three units) up to very long chain-like compounds called polymers. Polymers have a wide variety of properties depending on the specific chemistry, ranging from very durable, hard coatings to foams, adhesives and binders, and rubbery and elastic polymers (elastomers). An example of a polymer is polyurethane. Polyurethane is created when diisocyanates react with polyols (molecules containing at least two free hydroxyl groups).

Prepolymers possess free isocyanate groups prepared from the reaction of a polyol with an excess of di- or polyisocyanate. The most common HDI-based prepolymer used in polyurethane paints is isocyanurate (HDI-IC) and biuret (HDIB). Polyisocyanates are species possessing free isocyanate groups and derived from monomeric isocyanates by directly linking monomeric units (a homopolymer) or by reacting monomers with di- or poly-functional alcohols or amines. Oligomer isocyanates (oligomers) are relatively low molecular weight polyisocyanate (Reference b).

Polyureas are formed by a reaction of an isocyanate component with an amine component. Polyureas are high performance brushed or sprayed elastomers. They are extremely tough, monolithic membranes with excellent water and good chemical resistance. Modified polyureas or hybrids contain a combination of polyurethane and polyureas base ingredients and have been developed to achieve some application advantages of pure polyuria, but with the advantage of lower cost polyurethane ingredients. Two component polyureas systems are 100% solid with extremely rapid cure times (seconds with specialized heated applicators), and tend to be insensitive to moisture and temperature.

Low molecular weight diisocyanate monomers, such as HDI and TDI evaporate relatively rapidly, resulting in potential vapor exposures in the work environment. Polymers or prepolymers of these monomers have lower evaporation rates and therefore lower inhalation potential. Higher molecular weight isocyanates do not readily volatilize at ambient temperature, but are still an inhalation hazard if aerosolized or heated in the work environment.

Diisocyanate formulations contain only a small amount of unreacted monomers and a greater quantity of partially reacted polyisocyanates. From a workplace exposure standpoint, polymeric and prepolymer isocyanates will exist primarily an aerosols rather than vapors, especially when the product is sprayed, due to their high molecular weights.

In the workplace, the atmosphere may contain some free monomer and mainly polymeric (or prepolymer) isocyanates. The isocyanates released in the air will depend on vapor pressures, composition of the polymer, particle size distribution and other dust generated (i.e., condensation nuclei and coating of small particles with un-reacted material).

3. Health Effects

A variety of events and activities can lead to an isocyanate exposure such as during production, application, curing, or with an accidental spill or leakage. Exposure may also be experienced during the cleaning and maintenance of equipment and the off gassing of newly applied products that contain isocyanates. Thermal decomposition of polyurethane materials from heating, grinding, welding metal with polyurethane coating and cutting polyurethane foams with hot wire cutting method or drilling, soldering, sawing, or sanding of material containing polyurethane can also cause an exposure. Exposure to heated diisocyanates can be extremely hazardous due to the high vapor concentrations and the airborne particulate created during condensation.

Isocyanates (in all forms, i.e. monomers, prepolymeric and polyisocyanates species) exposure can cause skin, eye, nose, throat, and lung irritation. It can also lead to skin and lung sensitization. Some chronic decrement in lung function has been shown (Reference c). Sensitization is hyper-reactive (allergy-like) response to a substance and may develop as a result of a large single exposure or from repeated exposures at lower levels. A sensitized individual typically will react to concentrations of isocyanates below the various occupational limits.

Isocyanates have not been found to cause cancer in workers, however, TDI was found to cause cancer in some laboratory animals. A cancer warning therefore accompanies any TDI containing product (Reference d).

4. Occupational Exposure Limits

Currently, Occupational Safety and Health Administration (OSHA) (Reference e), National Institute for Occupational Safety and Health (NIOSH) (Reference f), and American Conference of Governmental Industrial Hygienist (ACGIH) (Reference g) have established occupational exposure limits (OELs) for several diisocyanate monomers but have yet to establish any limits for other types of isocyanates such as polyisocyanates, or for total isocyanates. It is imperative to capture polyisocyanates as well as diisocyanates to ensure a quantitative evaluation of the overall risk of exposure. There currently are no OELs established in the United States for total isocyanates. However, polyisocyanate exposures may be compared to the Oregon/Covestro OELs listed in Table 1.

Table 1

Source	OELs
Covestro (formerly Bayer Material Science) Homopolymer of Hexamethylene Diisocyanate (CAS # 28182-81-2)* (Reference h)	1.0 mg/m^3 STEL 0.5 mg/m^3 TWA
State of Oregon HDI-BT (CAS # 4035-89-6)** HDI-IC (CAS #28182-81-2)* (Reference i)	1.0 mg/m3 STEL 0.5 mg/m3 TWA

*In the Industrial Sampling Guide for Comprehensive Industrial Hygiene Laboratories (CIHL), Homopolymer of Hexamethylene Diisocyanate and HDI-IC, are known as Hexamethylene diisocyanate (HDI Oligomers) (CIHL West) and Hexamethylene Diisocyanates homopolymer (CIHL East)

** In the Industrial Sampling Guide for Comprehensive Industrial Hygiene Laboratories (CIHL), HDI-BT is known as Hexamethylene diisocyanates Biuret (HDIB) (CIHL East)

The isocyanate OELs were established using HPLC analysis. Gravimetric analysis is not recommended for isocyanates, as it captures any particulates not just isocyanates. Any results obtained by gravimetric analysis should not be compared to the OELs listed above.

Australia, Ireland, and the United Kingdom have set OELs (8 hr. TWA) of 20 µg/m^3 and a STEL of 70 µg/m^3 for workplace air. In addition, Finland has set a STEL of 35 µg/m^3 and Sweden has set OELs of 5 parts per billion (ppb) (8 hr. TWA) and 5-minute STEL of 10 ppb for workplace air. These limits are for total isocyanate, which includes monomeric and all polymeric (oligomeric, polyisocyanates, prepolymeric) isocyanates (Reference j). Due to the reactive nature of the isocyanate group, analysis in the workplace is commonly carried out by trapping isocyanates with a derivatization reagent to produce a stable derivative. This International Standard method is based upon the UK method for isocyanate determination (MDHS25/3), which includes the use of a glass impinger containing 1-(2-methoxyphenyl)piperazine (1,2-MP) absorbing solution backed with a filter impregnated with 1,2-MP reagent and analysis by high performance liquid chromatography (HPLC) (Reference j). The MDHS25/3 method for total isocyanates is not a NIOSH or OSHA approved method, therefore, sampling and/or testing is not recommended for total isocyanates.

5. Sampling and Analysis Methods

Today, there are various analytical methods and techniques available for the sampling and analysis of isocyanates in the workplace environment. Below are the current sampling and analytical methods that are used in the Navy for isocyanates.

a. OSHA 42 & OSHA 18 (Modified). This method is used for HDI (CAS 822-06-0) and HDI Oligomer (CAS 28182-81-2); MDI; 2,4-TDI; and 2,6-TDI. This method uses pretreated 37 millimeter (mm) Glass Fiber Filters (GFF) with p-nitrobenzyl-N-(n-propyl) amine (a nitro reagent) for air samples collected for isocyanate compounds. The sample are analyzed using an Ultra Performance Liquid Chromatography (UPLC) equipped with an ultraviolet (UV) and fluorescence detectors that will identify the urea derivative produced after

extraction with reverse phase conditions. The diisocyanates collected on the GFF react with the nitro reagent to derive the diisocyanate. The derivative will be extracted with a 90/10 (v/v) acetonitrile (ACN)/dimethyl sulfoxide (DMSO) solution.

b. OSHA 42. This method is used to sample and analyze HDI (CAS 822-06-0), 2,4-TDI (CAS 584-84-9), and 2,6-TDI (CAS 91-08-7). OSHA 42 utilizes pretreated 37 mm GFF treated with 1-(pyridyl) piperazine (1-2PP). It has been validated for the monomeric form of TDI, HDI, and MDI only. This method is best for sampling of the monomeric species that are in vapor form. If aerosols are to be collected using these methods, field desorption is required. Sampling is performed open face and analysis is performed by HPLC equipped with ultraviolet or fluorescence detection.

c. OSHA 47. This method is used to sample and analyze MDI (CAS 101-68-8). OSHA 47 utilizes pretreated 37 mm GFF with 1-(pyridyl) piperazine (1-2PP). It has been validated for the monomeric for of TDI, HDI, and MDI only. This method is best for sampling of the monomeric species that are in vapor form. If aerosols are to be collected using these methods, field desorption is required. Sampling is performed open face and analysis is performed by HPLC equipped with ultraviolet or fluorescence detection.

d. OSHA 47 & OSHA 18 (Modified). This method is used to sample MDI (CAS 101-68-8). This method uses pretreated 37 mm Glass Fiber Filters (GFF) with p-nitrobenzyl-N-(n-propyl) amine (a nitro reagent) for air samples collected for isocyanate compounds. The sample is analyzed using an Ultra Performance Liquid Chromatography (UPLC) equipped with an ultraviolet (UV) and fluorescence detectors that will identify the urea derivative produced after extraction with reverse phase conditions. The diisocyanates collected on the GFF react with the nitro reagent to derive the diisocyanate. The derivative will be extracted with a 90/10 (v/v) acetonitrile (ACN)/dimethyl sulfoxide (DMSO) solution.

e. OSHA PV2092. This method is used to sample and analyze IPDI (CAS 4098-71-9). OSHA PV2092 uses pretreated 37 mm GFF with 1-(pyridyl) piperazine (1-2PP). It has been validated for the monomeric form of TDI, HDI, and MDI only. This method is best for sampling of the monomeric species that are in vapor form. If aerosols are to be collected using these methods, field desorption is required. Sampling is performed open face and analysis is performed by HPLC equipped with ultraviolet or fluorescence detection.

f. OSHA PV2030. This method is used to sample and analyze HDIB (CAS 4035-89-6). This method uses GFF coated with 1-(2-pyridyl) piperazine (1-2PP) with an open face cassette. Samples are extracted with 90/10 acetonitrile/dimethyl sulfoxide and analyzed by HPLC using a UV or fluorescence detector.

g. OSHA PV2125. This method is used to sample and analyze HDI Homopolymer (CAS 288182-81-2). This method uses a glass fiber filters coated with 1.0 mg of 1-(2-pyridyl) piperazine (1-2PP) which are sampled in open-face cassettes. Samples are extracted with 90/10 acetonitrile/dimethyl sulfoxide and analyzed by liquid chromatography (LC) using an ultraviolet or fluorescence detector.

NOTE: The Comprehensive Industrial Hygiene Laboratories (CIHLs) must be contacted in order to obtain the coated filters required for sampling (Reference k).

6. Field Evaluation and Worker Protection Recommendations

The following recommendations are based on the referenced studies or documents and are intended to be prudent actions for inhalation and dermal exposure potentials considering the physical form of the exposure and the ability to quantitatively assess risk.

NOTE: Each worksite should be evaluated to determine the actual or potential exposure to physical or chemical hazards based on the process being performed.

a. Mixing and Brush Applications. Includes worksite/equipment cleanup if not aerosolized.

b. Spray Application (Including Workers in the Vicinity of Isocyanate Product Spray Operations). Includes the cleaning of the spray gun if aerosolized solvent is used.

NOTE: Spray operations using dual component isocyanate coating shall only be conducted in areas designed for that purpose, such as a spray paint booth or spray room which ensures adequate ventilation and explosion protection (Reference l).

c. Airborne Exposure Assessment. Evaluate vapor and aerosol exposures for the monomers or biuret that may be present in the isocyanate product. Also evaluate organic vapors that may be present (consult Reference k). Compare the results to the exposure limits of either Reference e, f, or g. Polyisocyanate results may be compared to the OEL of 1 mg/m^3 STEL, 0.5 mg/m^3 TWA (References h and i).

d. Personal Protective Equipment. Evaluate the process for potential skin contact and/or splash hazards. An example of an ensemble for mixing and brush application:
   (1) Full body disposable coveralls (Tyvek® or equivalent)
   (2) Gloves (butyl rubber, nitrile or Viton®)
   (3) Eye/face protection (chemical goggles/face shield if full face respirator is not required as based on air sampling assessments)
   (4) Rubber shoes or shoe covers whenever there is a chance of footwear contamination from spillage or splashing
   (5) Respirator as determined by airborne exposure assessments of isocyanate and other organic vapor components of the paint system.

NOTE: The OSHA respiratory protection requirements (Reference m and OPNAVINST 5100.23 Series (Reference n) authorize the selection of respiratory protection based on process evaluation, measured exposure levels and assigned protection factors. According to paragraph D.(6) of Reference o, where an effective change schedule is implemented, air-purifying gas and vapor respirators may be used for hazardous chemicals, including those with few or no warning properties. This means that air-purifying respirators can be used for protection against isocyanates where cartridge change-out schedules are established and implemented. The minimum protection would be an elastomeric half mask, air-purifying respirator equipped with organic vapor cartridges and N95 prefilters for exposures of isocyanates up to ten times the OEL.