Toluene diisocyanates: Human health tier II assessment

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Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Benzene, 1,3-diisocyanato-2-methyl-	91-08-7
Benzene, 2,4-diisocyanato-1-methyl-	584-84-9
Benzene, 1,3-diisocyanatomethyl-, homopolymer	9017-01-0
1,3-Diazetidine-2,4-dione, 1,3-bis(3-isocyanatomethylphenyl)-	26747-90-0
Benzene, 1,3-diisocyanatomethyl-	26471-62-5
1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(3-isocyanatomethylphenyl)-	26603-40-7

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

All six chemicals of this group are structurally related with free isocyanate functional groups. Benzene, 1,3-diisocyanatomethyl- (TDI mixture; CAS No: 26471-62-5) is a mixture of benzene, 1,3-diisocyanato-2-methyl- (2,6-TDI; CAS No: 91-08-7) and benzene, 2,4-diisocyanato-1-methyl- (2,4-TDI; CAS No: 584-84-9). Most toxicological data are available on the TDI mixture (CAS No: 26471-62-5) and assessing these chemicals as a group allows read-across of data from data rich members to data poor members. In certain cases, study details do not specify the exact test material used but specifies it as toluene diisocyanate.

Benzene, 1,3-diisocyanatomethyl-, homopolymer (CAS No: 9017-01-0), 1,3-diazetidine-2,4-dione, 1,3-bis(3-isocyanatomethylphenyl)- (CAS No. 26747-90-0) and 1,3,5-triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(3-isocyanatomethylphenyl)- (CAS No. 26603-40-7), while being polymers, contain unreacted isocyanate functional groups and also may contain or reversibly form toluene diisocyanate. Hence, these chemicals exhibit a similar toxicology profile to other chemicals of this group.

Import, Manufacture and Use

Australian

Three chemicals of this group are listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume between 1000 and 10000 tonnes. These are:

- benzene, 1,3-diisocyanato-2-methyl- (CAS No: 91-08-7);
- benzene, 2,4-diisocyanato-1-methyl- (CAS No: 584-84-9); and
- benzene, 1,3-diisocyanatomethyl- (CAS No: 26471-62-5).

The following Australian industrial uses were reported under previous mandatory and voluntary calls for information for these 3 chemicals.

The chemicals have reported commercial uses including:

Benzene, 1,3-diisocyanato-2-methyl- (CAS No: 91-08-7)

- polyurethane foam, resin, moulding and coatings manufacture;
- construction material additives;
- foaming agents; and
- process regulators.

Benzene, 2,4-diisocyanato-1-methyl- (CAS No: 584-84-9)

- in manufacture of polyurethane paints, mouldings, foam, adhesives, grouts, sealants, resins, fabric coatings and floor lacquers;
- in pastes/fluids for repair of metal, rubber and concrete;
- construction material additives; and
- process regulators.

Benzene, 1,3-diisocyanatomethyl- (CAS No: 26471-62-5)

- manufacture of polyurethane prepolymers, cast elastomers and resins, rigid and flexible polyurethane mouldings;
- trace amounts in industrial surface coatings and polyisocyanate paint catalyst; and
- foaming agents.

No specific Australian use, import, or manufacture information has been identified for:

- benzene, 1,3-diisocyanatomethyl-, homopolymer (CAS No: 9017-01-0);
- 1,3-diazetidine-2,4-dione, 1,3-bis(3-isocyanatomethylphenyl)- (CAS No. 26747-90-0); or
- 1,3,5-triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(3-isocyanatomethylphenyl)- (CAS No. 26603-40-7).

International

The following international uses have been identified through the European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers, the Organisation for Economic Cooperation and Development Screening information data set International Assessment Report (OECD SIAR), Galleria Chemica, Substances and Preparations in the Nordic countries (SPIN) database, the European Commission Cosmetic Ingredients and Substances (CosIng) database, United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) dictionary & eChemPortal—OECD High Production Volume chemical program (OECD HPV), the US Environmental Protection Agency's (EPA) Aggregated Computer Toxicology Resource (ACToR), US Environment Protection Agency Action Plan on Toluene Diisocyanate and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The majority of chemicals of this group have the following reported uses which may include domestic applications including:

- adhesives and binding agents;
- fillers;
- floor coatings and sealants;
- paints, lacquers and varnishes; and
- surface treatment.

The majority of chemicals of this group have the following reported commercial uses including:

- in the manufacture of polyurethane foams, elastomers and coatings;
- construction materials;
- foaming agents;
- process regulators; and
- solvents.

The majority of chemicals of this group have the following reported site-limited use:

- as an intermediate.

Some chemicals of the group have the following reported uses including:

- colouring agents;
- reprographic agents;
- impregnation materials; and
- heat transferring agents.

Restrictions

Australian

Chemicals of this group, belonging to the group 'Isocyanates', are listed in the Poisons Standard (Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)). "ISOCYANATES, free organic, boiling below 300 °C, **except** in: (a) viscous polyurethane adhesives; or (b) viscous polyurethane sealants; containing not more than 0.7 per cent of free organic isocyanates boiling below 300 °C" are on Schedule 6 of the SUSMP.

Schedule 6 chemicals are labelled with ‘Poison’. These are substances with a moderate potential for causing harm, the extent of which can be reduced by using distinctive packaging with strong warnings and safety directions on the label.

Chemicals of this group are listed in the Safe Work Australia, Model Work Health and Safety Regulations, Hazardous chemicals (other than lead) requiring health monitoring (Safe Work Australia 2011).

International

Canada List of Prohibited and Restricted Cosmetic Ingredients (The Cosmetic Ingredient Hotlist).

EU Cosmetic Directive 76/768/EEC Annex II: List of Substances which must not form part of the Composition of Cosmetic Products.

European Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food - Annex I: Substances. Restriction imposed at 1 mg/kg in final product expressed as isocyanate moiety.

New Zealand Cosmetic Products Group Standard - Schedule 4: Components Cosmetic Products Must Not Contain - Table 1.

Existing Worker Health and Safety Controls

Hazard Classification

Some of the chemicals (CAS No. 91-08-7, 584-84-9 and 26471-62-5) of this group are classified as hazardous with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

Xn; R40 (Carcinogenicity Cat. 3)

T+; R26 (Acute toxicity)

Xi; R36/37/38 (Irritation)

Xn; R42/43 (Sensitisation)

Exposure Standards

Australian

The chemicals of this group have exposure standards of 0.02 mg/m³ time weighted average (TWA) and 0.07 mg/m³ short term exposure limit (STEL) as isocyanates, all (as-NCO).

International

The following exposure standards are identified (Galleria Chemica):

An exposure limit (STEL) of 0.021 – 0.14 mg/m³ in countries such as France, Greece, Hungary, Iceland, Spain and South Africa.

An exposure limit (TWA) of 0.007 – 0.07 mg/m³ in countries such as Denmark, Greece, Hungary, Japan, Poland, South Africa, Spain, United Kingdom and USA.

Health Hazard Information

Toxicokinetics

Oral dosing of toluene diisocyanate results in breakdown to toluene diamine and its salts under acidic conditions in the stomach (Bolognesi et al., 2001). Following inhalation exposure to 14C-toluene diisocyanate rapid absorption was observed with levels of radioactivity in blood proportional to the exposure concentration (Collins, 2010). The majority of the radiolabel was conjugated to proteins in the plasma. Inhaled toluene diisocyanate is largely excreted in urine as acetylated amine metabolites.

Acute Toxicity

Oral

The chemicals of this group exhibit low acute toxicity in animal tests as evidenced by reported oral LD50s in rat studies. LD50s ranged from 3060 - 5620 mg/kg bw (REACH Dossier, 2013b; IPCS, 1987). Observed sub-lethal effects included laboured breathing, inactivity, diarrhoea and weight loss.

Dermal

The chemicals of this group exhibit low acute toxicity in animal tests as evidenced by a reported dermal LD50 of >9400 mg/kg bw in rabbits (REACH Dossier, 2013b). Observed sub-lethal effects included dermal irritation.

Inhalation

The chemicals of this group are classified as hazardous with the risk phrase ‘Very toxic by inhalation’ (T+; R26) in HSIS (Safe Work Australia). The data available (median lethal concentration (LC50) is 0.48 mg/L for 1 hour exposure) support this classification (REACH Dossier 2013b). Reported signs of toxicity include haemorrhagic lungs, wheezing and body weight loss.

Observation in humans

IPCS (1987) reports that the symptoms of acute exposure are non-specific. These include: "irritation of the nose and throat, shortness of breath, choking, coughing, retrosternal discomfort or pain, and gastrointestinal stress (e.g., nausea, vomiting, and abdominal pain)". The onset of these symptoms could be delayed following exposure, and may persist for days, months, or years following acute exposure.

Corrosion / Irritation

Respiratory Irritation

The chemicals of this group are classified as hazardous with the risk phrase 'Irritating to respiratory system' (Xi; R37) in HSIS (Safe Work Australia). The available data support this classification.

IPCS (1987) reported that occupational exposure to toluene diisocyanates produces a range of respiratory effects including irritation of the upper and lower respiratory tract. Respiratory irritation has been reported to occur in humans at levels ranging between 0.712 and 3.560 mg/m³.

In a range of repeat dose toxicity studies with durations of 30 days to two years in rats and hamsters, local irritation of the nasal cavity, larynx, trachea and lungs was evident at concentrations of 0.05 - 2.83 ppm.

Skin Irritation

The chemicals of this group are classified as hazardous with the risk phrase 'Irritating to skin' (Xi; R38) in HSIS (Safe Work Australia). The available data support this classification.

Toluene diisocyanate on unabraded rabbit skin produced erythema and oedema after a four hour semi-occlusive exposure (REACH Dossier, 2013b). The mean erythema and oedema scores over the reading times (24, 28 and 72 hours) were 2.66 and 1.55, respectively. After 13 days, the exposed areas had effects which were not completely reversible.

Eye Irritation

The chemicals of this group are classified as hazardous with the risk phrase 'Irritating to eyes' (Xi; R36) in HSIS (Safe Work Australia). The available data support this classification.

In an eye irritation study in rabbits, toluene diisocyanate was found to be irritating with redness of the conjuctivae (conjunctivitis) and oedema of the conjuctivae (chemosis) observed at 24, 48 and 72 hours (REACH Dossier 2013b). The mean conjunctivitis and chemosis scores over the reading times (24, 28 and 72 hours) were 3 and 4, respectively. Effects were reversible within the 21 day observation period.

Observation in humans

IPCS (1987) reported that occupational eye exposure to toluene diisocyanate resulted in mild irritation, characterised by itching and lachrymation, progressing to conjunctivitis and keratoconjunctivitis.

Sensitisation

Respiratory Sensitisation

The chemicals of this group are classified as hazardous with the risk phrase 'May cause sensitisation by inhalation' (Xn; R42) in HSIS (Safe Work Australia). The available data support this classification.

In humans, inhalation exposure results in toluene diisocyanate-induced asthma, which may continue for several years after the removal of the exposure (IPCS, 1987). It has been reported that a challenge at 1 ppb (0.007 mg/m^3) toluene diisocyanate induces asthma in previously sensitised subjects (Environment and Health Canada, 2008). In participants not suffering from occupational asthma, in controlled experiments, sensitisation occurred at levels at 10 ppb (0.07 mg/m^3).

Deaths related to exposure to diisocyanate in sensitised people have been cited in US EPA (2011).

Skin Sensitisation

The chemicals of this group are classified as hazardous with the risk phrase 'May cause sensitisation by skin contact' (Xi; R43) in HSIS (Safe Work Australia). A positive result reported in a local lymph node assay [estimated concentration three (EC3) is 0.02% (w/v)] with toluene diisocyanate supports this classification (REACH Dossier, 2013b).

Skin sensitisation on repeated exposure to toluene diisocyanates has also been reported in humans (IPCS, 1987; Environment and Health Canada, 2008).

Repeated Dose Toxicity

Oral

Systemic toxicity is expected following repeated oral exposure to chemicals of this group, as they break down to toluene diamine and its salts under the acidic conditions in the stomach. Although the lowest observed effect level (LOEL) from a 28 day rat study was 30 mg/kg bw/day, the effects were reversible following removal of the exposure. The 13 week rat study showed adverse effects at or above 60 mg/kg bw/day (no observed adverse effect level (NOAEL) = 30 mg/kg bw/day in males). Based on the data available, the chemicals of this group are not considered to cause serious damage to health by repeated oral exposure.

In a repeat dose toxicity study benzene, 1,3-diisocyanatomethyl- (CAS No. 26471-62-5) was administered by oral gavage in corn oil to Fischer 344 rats five times per week for 13 weeks at dose levels of 0, 15, 30, 60, 120 or 240 mg/kg bw/day (REACH Dossier, 2013b). One treatment related death was observed in female rats at 240 mg/kg bw/day. Observed systemic effects included a depression in body weight gain in males treated at 60 mg/kg bw/day and higher and in females treated at 120 mg/kg

bw/day and higher. Depression in body weight gain was biologically significant at the highest dose in males. Histopathological investigation showed a dose related accumulation of mucoid material in the pulmonary bronchioles in males treated at 60 mg/kg bw/day and higher and in females treated at 120 mg/kg bw/day and higher. The NOAEL for males was 30 mg/kg bw/day and for females 60 mg/kg bw/day.

In a 28 day repeated dose toxicity study, benzene, 1,3-diisocyanatomethyl- (CAS No. 26471-62-5) was administered by oral gavage in corn oil to Sprague Dawley (SD) rats at dose levels of 30, 100 or 300 mg/kg bw/day (REACH Dossier, 2013b). Histopathological changes were seen in lungs (males at =100 mg/kg bw/day; females at = 30 mg/kg bw/day), trachea (both sexes at = 30 mg/kg bw/day), stomach (both sexes at 300 mg/kg bw/day), liver (both sexes at 300 mg/kg bw/day) and spleen (both sexes at 300 mg/kg bw/day). It was reported that after a recovery period of 14 days all changes in lungs, trachea, stomach, small intestine and liver were reversible. The LOAEL was 30 mg/kg bw/day based on histopathological changes in lungs (females) and trachea (males and females).

Dermal

No data are available.

Inhalation

Effects observed with repeated inhalation exposure are predominately those of local irritation and sensitisation. Based on the available information, systemic toxicity is not expected following repeated inhalation exposure of chemicals belonging to this group.

In a range of repeated dose toxicity studies with durations of 30 days to two years in rats, mice and hamsters, local irritation of the nasal cavity, larynx, trachea and lungs was the predominant effect (REACH Dossier, 2013b). In addition, body weight gain was reduced in almost all studies. In a two year rat study the NOAEC for males was 0.05 ppm and LOAEC for females was 0.05 ppm, with regard to histopathological changes of the anterior nasal cavity.

Environment and Health Canada (2008) reported that the lowest observed effect concentration (LOEC) for decreased lung function in humans in a prospective occupational study was 1.9 ppb (equivalent to 0.014 mg/m³).

Genotoxicity

The genotoxicity potential of chemicals of this group is equivocal, based on the available data. However, potential breakdown of toluene diisocyanate to toluenediamine (TDA) in the stomach could suggest potential for genotoxicity through the oral route, depending on the metabolic fate of toluene diisocyanate and the degree of TDA formation.

Toluene diisocyanate gave positive results in several in vitro genotoxicity studies (IPCS 1987; IARC 1999; Bolognesi et al., 2001). The in vitro studies are difficult to interpret given that toluene diisocyanate degrades to TDA in the presence of vehicles such as dimethylsulfoxide (DMSO) and ethyleneglycol-dimethylether (EDGE) (Bolognesi et al., 2001). TDA is a well known mutagen.

Toluene diisocyanate induced sex linked recessive lethal mutations and reciprocal translocations in *Drosophila* studies (Bolognesi et al., 2001). However, toluene diisocyanate was negative in a micronucleus assay in bone marrow of rats and mice following a four week inhalation exposure (6 hours per day and five days per week) to 0.05 and 0.15 ppm.

Carcinogenicity

The chemicals of this group are classified as hazardous as Category 3 carcinogens with the risk phrase 'Limited evidence of a carcinogenic effect' (Xn; R40) in HSIS (Safe Work Australia). The available data support this classification.

The International Agency for Research on Cancer (IARC) has classified the chemical as ‘possibly carcinogenic to humans’ (Group 2B), based on inadequate evidence for carcinogenicity in humans, but sufficient evidence for carcinogenicity based on animal testing.

IARC (1999) reported that there is no strong association or consistent pattern in toluene diisocyanate being responsible for carcinogenicity in humans in three industrial cohort studies and in a population based case-control study.

In a two year carcinogenicity study in rats, toluene diisocyanate administered by gavage induced a dose-dependent increase in the incidence of subcutaneous fibromas and fibrosarcomas (combined) and an increased incidence of pancreatic acinar cell adenomas at the two treatment doses of 30 and 60 mg/kg bw/day, in male rats and at the highest dose tested in female rats (120 mg/kg bw/day) (IARC, 1999; REACH Dossier, 2013b). In female rats, an increased incidence of mammary gland tumours, pancreatic islet-cell adenomas and neoplastic nodules of the liver were also observed at the two treatment doses of 60 and 120 mg/kg bw/day (IARC, 1999; REACH Dossier, 2013b).

In a two year mouse study, toluene diisocyanate administered by gavage induced a dose dependent increase in the incidence of haemangiomas and haemangiosarcomas (combined) and hepatocellular adenomas at the highest dose tested (120 mg/kg bw/day in female mice) (IARC, 1999; REACH Dossier, 2013b). IARC (1999) reported that no treatment related tumours were seen in male animals possibly due to poor survival.

No treatment related tumours were seen in animal studies where the inhalation route of exposure was used (IARC, 1999). IARC (1999) reported some deficiencies in the original reporting of the inhalation study.

Reproductive and Developmental Toxicity

No reproductive toxicity effects were observed and developmental effects were only observed secondary to maternal toxicity. Therefore, chemicals of this group are not considered to be specific reproductive or developmental toxins.

In a well conducted two generation reproductive toxicity study (OECD TG 416), toluene diisocyanate was administered as a vapour at concentrations of 0, 0.02, 0.08 or 0.30 ppm (corresponding to 0, 0.15, 0.58, 2.18 mg/m^3) (REACH Dossier, 2013b). Toxicity in F0 animals was evident at 0.08 and 0.3 ppm. Toxicity included nasal discharge, reduced weight gains and nasal passage inflammation (rhinitis). No treatment related effects on reproductive parameters in any generation were observed (Collins, 2002; REACH Dossier, 2013b). Hence, the reproductive NOAEC was >0.3 ppm.

In a well conducted developmental study (OECD TG 414), toluene diisocyanate was administered as a vapour to female rats for six hours per day on gestational day six to 15, at concentrations of 0, 0.02, 0.1 or 0.5 ppm (REACH Dossier, 2013b). Maternal toxicity was observed at the highest dose with a significant decrease in body weight gain and audible respiration. No treatment related effects in litter size and weights, number of viable foetuses, or sex ratio were evident. However, a common rat skeletal variation was observed in foetuses, at the maternally toxic dose of 0.5 ppm, where the cervical centrum 5 was poorly ossified. The reported maternal and developmental toxicity NOAEC was 0.1 ppm.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include respiratory sensitisation with sufficient severity to lead to mortality in sensitised people. Other health effects include a systemic long term effect (carcinogenicity), a systemic acute effect (acute toxicity by the inhalation route of exposure) and local effects (skin sensitisation and respiratory irritation). The chemicals of this group may also cause skin and eye irritation.

Public Risk Characterisation

Although no consumer uses have been identified in Australia, chemicals of this group are known to be used in products of the type which may have domestic use (eg. adhesives, binding agents and floor sealants) overseas. Inhalation and dermal routes are the likely routes of exposure for the public through the consumer use of products containing chemicals of this group. Articles, such as polyurethane products, manufactured from toluene diisocyanate are considered to be completely cured and hence, considered non-toxic (US EPA 2011). When completely cured, free isocyanate functional groups are not available for reaction.

In Australia, the chemicals of this group are currently listed on Schedule 6 of the SUSMP. A strong warning statement, safety directions and first aid instructions apply to any domestic products containing chemicals of this group. The current controls are considered adequate to minimise the risk to public health posed by any domestic use of these chemicals. Therefore, the risk to public health is not considered to be unreasonable.

Occupational Risk Characterisation

During formulation of products, dermal, ocular and inhalation exposure of workers to chemicals of this group may occur particularly where manual or open processes are used. These may include transfer and blending activities, quality control analysis and cleaning and maintenance of equipment. Worker exposure to these chemicals at lower concentrations may also occur during use of formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed. Exposure to TDA from ingestion of toluene diisocyanate is unlikely given the controls that should be in place to limit exposure to inhalation and dermal contact.

Given the critical health effects of the chemicals of this group, the chemicals may pose an unreasonable risk to workers if adequate control measures to minimise dermal, ocular or inhalation exposure are not implemented. The chemicals should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace has adequate information to determine appropriate controls. Based on the available data the hazard classification in HSIS is considered appropriate.

NICNAS Recommendation

Current risk management measures are considered adequate for the protection of public and workers' health and safety provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory. No further assessment is required.

Regulatory Control

Public Health

Products containing the chemicals of this group should be labelled in accordance with state and territory legislation (SUSMP).

Work Health and Safety

The chemicals of this group are recommended for classification and labelling under the current approved criteria and adopted Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Very toxic by inhalation (T+; R26)*	Fatal if inhaled - Cat. 1 (H330)
Irritation / Corrosivity	Irritating to eyes (Xi; R36)* Irritating to skin (Xi; R38)* Irritating to respiratory system (Xi; R37)*	Causes serious eye irritation - Cat. 2A (H319) Causes skin irritation - Cat. 2 (H315) May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Sensitisation	May cause sensitisation by inhalation (Xn, R42)* May cause sensitisation by skin contact (Xi; R43)*	May cause allergy or asthma symptoms or breathing difficulties if inhaled - Cat. 1 (H334) May cause an allergic skin reaction - Cat. 1 (H317)
Carcinogenicity	Carc. Cat 3 - Limited evidence of a carcinogenic effect (Xn; R40)*	Suspected of causing cancer - Cat. 2 (H351)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for consumers

Products containing chemicals of this group should be used according to label instructions.

Advice for industry

Control measures

Control measures to minimise the risk from dermal, ocular and inhalation exposure to chemicals of this group should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storage, handling and use of a hazardous chemical are dependent on the physical form and the manner in which the chemical is used. Examples of control measures which may minimise the risk include but are not limited to:

- use of closed systems or isolation of operations;
- use of local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimisation of manual processes and work tasks through automation of processes;
- work procedures that minimise splashes and spills;
- regular cleaning of equipment and work areas; and
- use of protective equipment that is designed, constructed, and operated to ensure that, the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing Risks of Hazardous Chemicals in the Workplace—Code of Practice* available on the Safe Work Australia website.

Personal protective equipment should not be relied upon on its own to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selection of personal protective equipment can be obtained from Australia, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of hazardous chemical are prepared; and
- management of risks arising from storage, handling and use of a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare a (m)SDS and how to label containers of hazardous chemicals are provided in relevant Codes of Practice such as the *Preparation of Safety Data Sheets for Hazardous Chemicals— Code of Practice* and *Labelling of Workplace Hazardous Chemicals—Code of Practice*, respectively. These Codes of Practice are available from the Safe Work Australia website

A review of physical hazards of chemicals of this group has not been undertaken as part of this assessment.

References

Approved Criteria for Classifying Hazardous Substances [NOHSC: 1008(2004)] Third edition. Accessed at **http://www.nohsc.gov.au/pdf/Standards/approved_criteriaNOHSC1008_2004.pdf**

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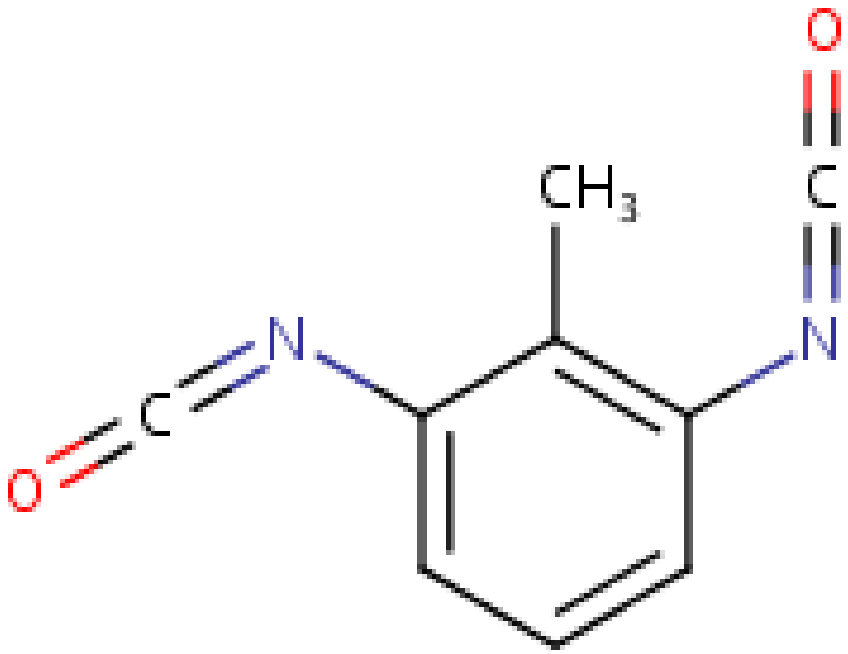
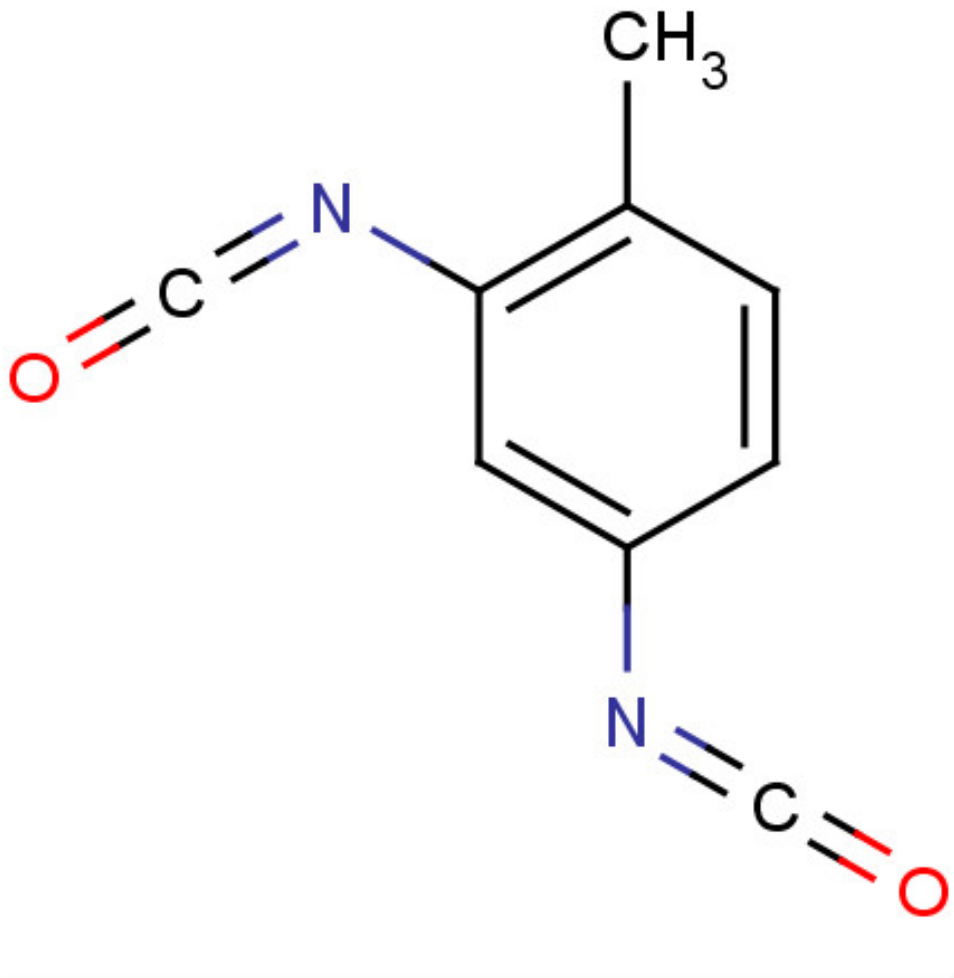
Last Update 22 March 2013

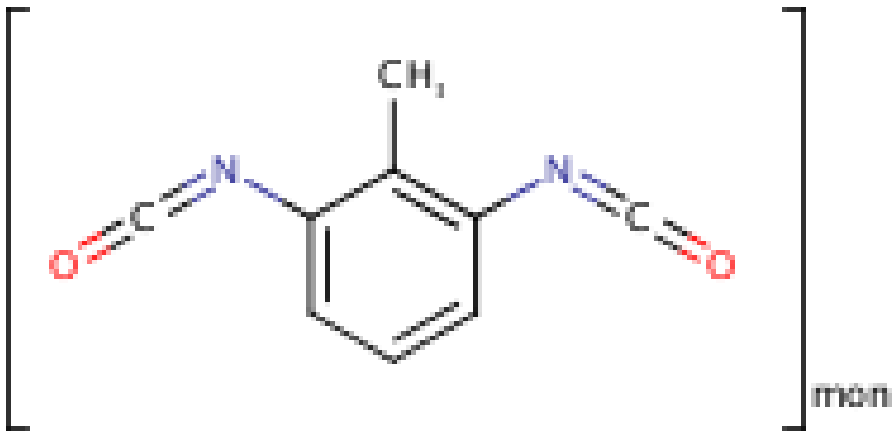
Chemical Identities

Chemical Name in the Inventory and Synonyms	**Benzene, 1,3-diisocyanato-2-methyl-** Toluene-2,6-diisocyanate Isocyanic acid, 2-methyl-m-phenylene ester 2,6-TDI 2-Methyl-meta-phenylene isocyanate 2-Methyl-m-phenylene diisocyanate
CAS Number	91-08-7
Structural Formula	
Molecular Formula	C9H6N2O2
Molecular Weight	174.16

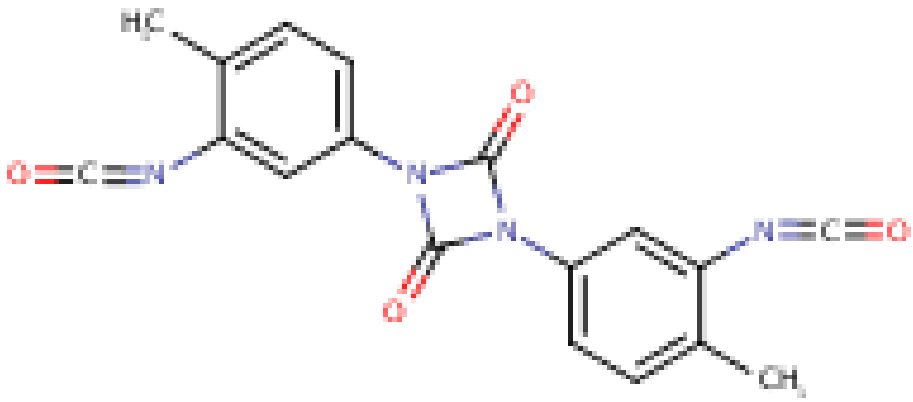
Chemical Name in the Inventory and Synonyms	**Benzene, 2,4-diisocyanato-1-methyl-** Toluene-2,4-diisocyanate 4-methyl-m-phenylene diisocyanate 2,4-TDI

	4-Methyl-meta-phenylene diisocyanate 1,3-Diisocyanato-4-methylbenzene
CAS Number	584-84-9
Structural Formula	
Molecular Formula	C9H6N2O2
Molecular Weight	174.16

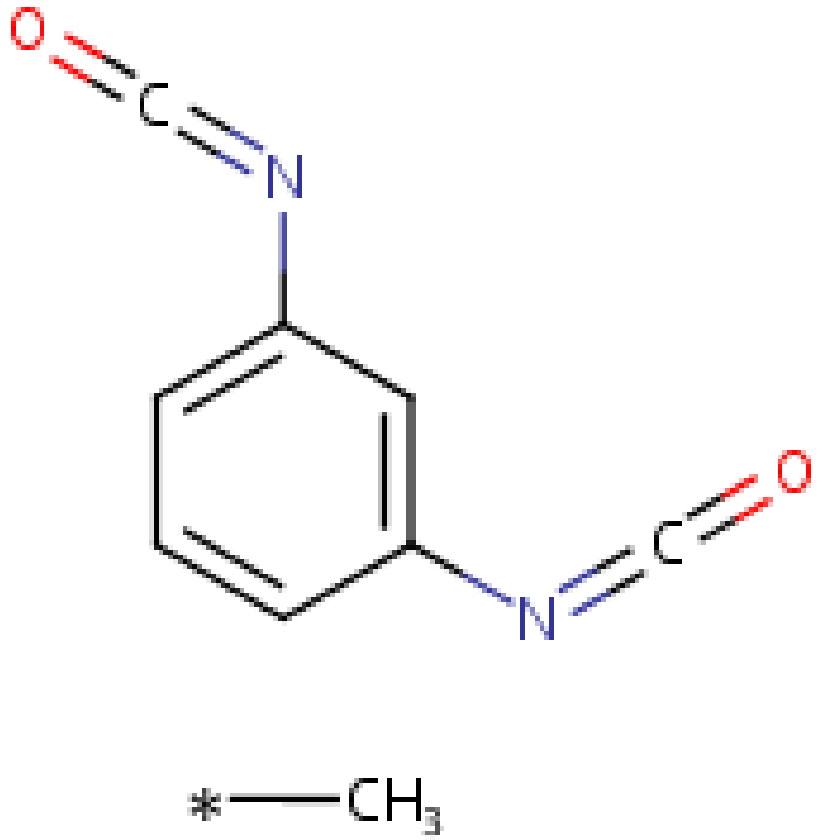
Chemical Name in the Inventory and Synonyms	**Benzene, 1,3-diisocyanatomethyl-, homopolymer** Tolylene diisocyanate, homopolymer Toluene diisocyanate homopolymer TDI homopolymer Methyl-m-phenylene isocyanate polymer
CAS Number	9017-01-0
Structural Formula	

	
Molecular Formula	(C9H6N2O2)x
Molecular Weight	174.16

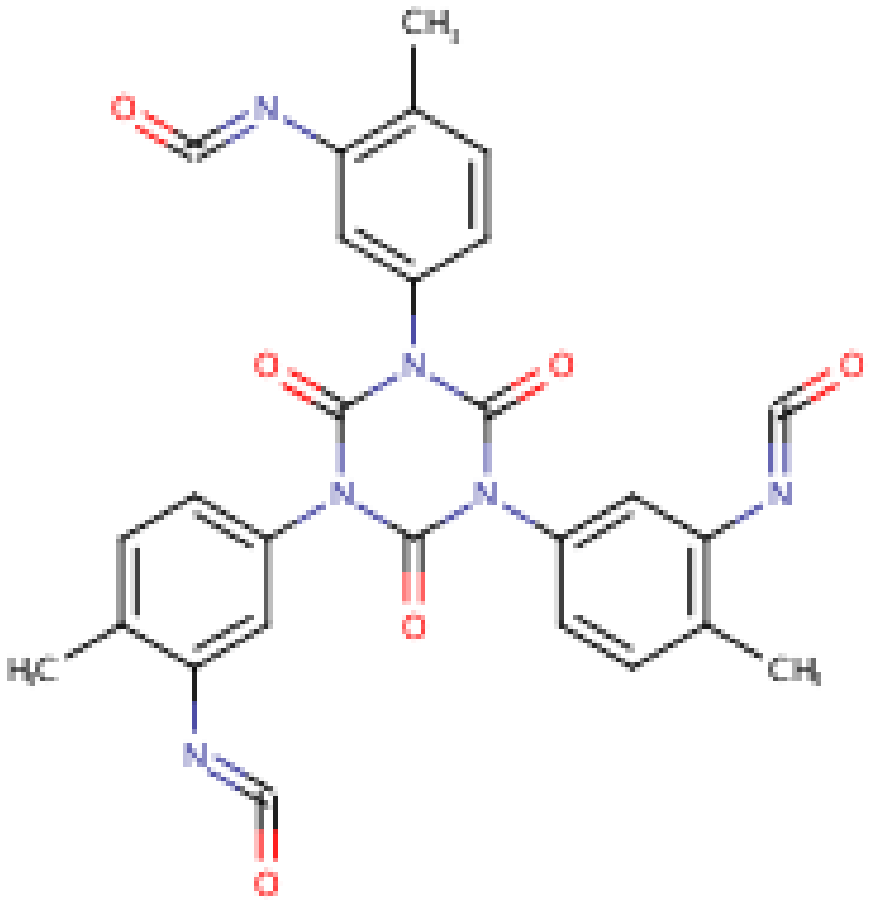
Chemical Name in the Inventory and Synonyms	**1,3-Diazetidine-2,4-dione, 1,3-bis(3-isocyanatomethylphenyl)-** Toluene diisocyanate, dimer 2,4-Dioxo-1,3-diazetidine-1,3-bis(methyl-m-phenylene) diisocyanate 2,4-Toluenediisocyanate dimer 2,4-Tolylene diisocyanate dimer
CAS Number	26747-90-0
Structural Formula	

	
Molecular Formula	C18H12N4O4
Molecular Weight	348.32

Chemical Name in the Inventory and Synonyms	**Benzene, 1,3-diisocyanatomethyl-** Toluene diisocyanate Methylphenylene isocyanate m-tolylidene diisocyanate
CAS Number	26471-62-5
Structural Formula	

	
Molecular Formula	C9H6N2O2
Molecular Weight	174.16

Chemical Name in the Inventory and Synonyms	**1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(3-isocyanatomethylphenyl)-** 2,4-Toluene diisocyanate trimer 2,4-Tolylene diisocyanate isocyanurate trimer Tolylene diisocyanate trimer
CAS Number	26603-40-7
Structural Formula	

	
Molecular Formula	C27H18N6O6
Molecular Weight	522.48

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