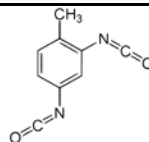


## Stofdocument deel A

CAS-nr: 584-84-9 **Tolueen-2,4-diisocynaat**  
C<sub>9</sub>H<sub>6</sub>N<sub>2</sub>O<sub>4</sub>



VN-nr: 2078

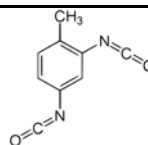
GEVI: 60

**Synoniemen:** 2,4-TDI, 2,4-tolueendiisocynaat, 4-methyleen-m-fenyleendiisocynaat  
(Engels: Toluene 2,4-Diisocyanate)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	<b>VRW (mg/m<sup>3</sup>)</b>	0,15	0,15	0,15	0,073	0,073	0,073
Alarmeringsgrenswaarden	<b>AGW (mg/m<sup>3</sup>)</b>	1,7	1,2	0,60	0,30	0,15	0,15
Levensbedreigende waarden	<b>LBW (mg/m<sup>3</sup>)</b>	6,8	4,7	3,7	3,0	2,3	1,2
Datum vaststelling: 24-09-2009		1 mg/m <sup>3</sup> = 0,138 ppm; 1 ppm = 7,25 mg/m <sup>3</sup>					
<b>Explosiegrens: LEL = 0,9 vol% ≈ 65 000 mg/m<sup>3</sup></b>		<b>Geur:</b> zoete, fruitige, scherpe geur <b>LOA:</b> niet afgeleid					
Fysisch-chemische eigenschappen				Overige informatie			
<b>Uiterlijk:</b> heldere, lichtgele vloeistof of kristallen		Molecuulmassa: 174,2 g/mol		Publieke grenswaarde: niet afgeleid			
<b>Brand:</b> brandbaar, bij vele reacties kans op brand en explosie		Zuurgraad: Geen data		MAK: niet afgeleid			
<b>Relatieve dichtheid van verzadigd damp-luchtmengsel:</b> 1,0		LogKow: Geen data		TLV-TWA: 0,007 mg/m <sup>3</sup>			
		Wateroplosbaarheid: Reactie					
		Verzadigde dampdruk: 0,04 mbar					
Toxicologische eigenschappen							
<b>Effecten bij inhalatoire blootstelling</b>				<b>Toxiciteit bij eenmalige, inhalatoire blootstelling</b>			
<u>Onder VRW:</u> mogelijk lichte irritatie				<ul style="list-style-type: none"> <li>Tolueen-2-4-diisocynaat is sterk irriterend voor de ogen en luchtwegen. Bij hoge concentraties werkt tolueen-2,4-diisocynaat bijtend.</li> <li>Bij hoge concentraties kan tolueen-2,4-diisocynaat longontsteking (chemische pneumonitis) en longoedeem veroorzaken, waarbij de verschijnselen pas na enkele uren kunnen optreden en worden versterkt door lichamelijke inspanning.</li> <li>Blootstelling kan een astmatische reactie veroorzaken.</li> <li>De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact. Kruisgevoeligheid met andere diisocyanaten is mogelijk.</li> </ul>			
<u>VRW → AGW:</u> irritatie aan ogen, neus en luchtwegen, keelpijn, hoesten, rhinitis, tranenvloed, hoofdpijn							
<u>AGW → LBW:</u> ernstige luchtwegirritatie, onregelmatige ademhaling, benauwdheid, longoedeem, bloed ophoesten							
<u>Boven LBW:</u> ademnood, sterfte							
<b>Effecten bij blootstelling aan vloeistof</b>				<b>Carcinogeniteit</b>			
<u>Huidcontact:</u> bijtend, roodheid en pijn, blaren				IARC classificatie tolueen diisocyanaten: 2B			
<u>Oogcontact:</u> bijtend, roodheid, pijn				CRP: niet afgeleid			
Beknopte medische informatie							
<b>Ontsmetting damp</b>							
<i>algemeen:</i> frisse lucht, rust, halfzittende houding en onmiddellijk arts raadplegen.							
<i>ogen:</i> desgewenst uitspoelen met water (evt. contactlenzen verwijderen).							
<b>Ontsmetting vloeistof</b>							
<i>huid:</i> overmaat stof opdeppen, verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.							
<i>ogen:</i> minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.							
<i>inslikken:</i> mond laten spoelen (uitspugen!), GEEN braken opwekken en arts raadplegen.							
<b>Specifieke behandeling en materialen:</b> geen.							
Neem contact op met het NVIC (Tel: 030 - 274 8888) voor informatie met betrekking tot medisch handelen							

## Stofdocument deel B

CAS-nr: 584-84-9 **Toluene 2,4-diisocyanate**  
C<sub>9</sub>H<sub>6</sub>N<sub>2</sub>O<sub>4</sub>



UN-nr: 2078

### Basis for the Dutch Intervention Values

**VRW:** AEGL values are adopted, 2 h value added

**AGW:** AEGL values are adopted (except 10 min value for which time scaling was applied), 2 h value added

**LBW:** AEGL values are adopted, (except 10 min value for which time scaling was applied), 2 h value added

Date: 24-09-2009

AEGL document: Final, 2004

### Dutch Intervention Values (mg/m<sup>3</sup>)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
<b>VRW</b>	0.15	0.15	0.15	0.073	0.073	0.073	Light irritation (nose and throat), chest tightness in exposed humans
<b>AGW</b>	1.7	1.2	0.60	0.30	0.15	0.15	Irritation eyes and respiratory tract (humans)
<b>LBW</b>	6.8	4.7	3.7	3.0	2.3	1.2	Lethality animals

### Derivation of the Dutch Intervention Values

**VRW:** A human volunteer study with healthy and asthmatic individuals was used as starting point for the derivation of the VRW values. Volunteers were exposed to a mixture of 2,4-TDI and 2,6-TDI in a ratio of 80:20, respectively. Asthmatic individuals tolerated exposures of 0.01 ppm (0.073 mg/m<sup>3</sup>) for one hour followed by a rest period of 45 minutes and a second exposure to 0.02 ppm (0.15 mg/m<sup>3</sup>) for another hour. Healthy adults (control group) were exposed for 2 hours at 0.02 ppm (0.15 mg/m<sup>3</sup>). Both groups reported eye and throat irritation, cough, chest tightness, rhinitis, dyspnea and/or headache. There was no indication whether the effects were worse in asthmatics at the 0.01 ppm or 0.02 ppm (0.073 and 0.15 mg/m<sup>3</sup>, respectively) level. Therefore, the 0.02 ppm (0.15 mg/m<sup>3</sup>) was identified as the basis of for the 10-, 30-min and 1-hour time points and the 0.01 ppm (0.073 mg/m<sup>3</sup>) concentration was identified as basis for the 2-, 4- and 8-hour time points. Because asthmatic subjects tolerated 0.02 ppm (0.15 mg/m<sup>3</sup>) for 1 hour after pre-exposure at 0.01 ppm (0.073 mg/m<sup>3</sup>), it is assumed that the asthmatic population could tolerate the lower concentration for a longer duration. No additional uncertainty factors were applied, because a human study was used as starting point and because asthmatic persons are considered a sensitive population. However, it is recognized that individuals with pre-existing allergic sensitization to this substance might not be protected at those concentrations and might experience airway reactivity with symptoms characteristic of an asthmatic attack, such as coughing, wheezing, chest tightness, and difficulty in breathing. The 0.01 ppm (0.073 mg/m<sup>3</sup>) exposure concentration for the longer time periods is reasonable because data suggest that the adverse health effects of inhaled 2,4-TDI are concentration dependent rather than concentration × time dependent. The proposed values are supported by the fact that in an additional study healthy subjects tolerated approximately 0.01 ppm (0.073 mg/m<sup>3</sup>) for 4 hours with no adverse effects while a slightly higher concentration of 0.03 ppm (0.22 mg/m<sup>3</sup>) resulted in symptoms similar to the point of departure study in 100% of workers at a manufacturing plant.

**AGW:** Humans exposure to 0.5 ppm (3.63 mg/m<sup>3</sup>) 2,4-TDI for 30 minutes resulted in eye and throat irritation and lacrimation. The next higher concentration of 1.3 ppm (9.4 mg/m<sup>3</sup>) was intolerable after 10 minutes. A 30 minute exposure to 3.63 mg/m<sup>3</sup> was used as point of departure for deriving AGW values. Although ocular and respiratory tract irritation associated with 2,4-TDI exposure appears to be more concentration dependent than duration dependent, longer exposure periods can result in excessive fluid accumulation in the respiratory tract, which could lead to more severe consequences than defined under AGW. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. Time scaling was done using the equation  $C^n \times t = k$ , with the default values of n=1 and n=3 for extrapolation to longer and shorter durations, respectively. The 4-hr value was used for the 8-hour time point, because extrapolation to 8-hr resulted in a concentration similar to one that caused only mild effects in workers exposed for more than 7 hours and on 8-hour work shifts.

**LBW:** Several lethality studies in different species are available. A 4-hour lethality study in mice appeared to provide the lowest LC<sub>50</sub> value, viz. 9.7 ppm (70 mg/m<sup>3</sup>). The specific TDI isomers studied were not identified. This value was taken as point of departure and was divided by 3 to estimate a threshold of lethality of 3.2 ppm (23 mg/m<sup>3</sup>). Extrapolation of the probit regression line, obtained from a graph in the selected study, shows that a concentration of approximately 4 ppm would result in 1% lethality. Therefore, one-third of the LC<sub>50</sub> is considered to be a reasonable estimate of the threshold for lethality. A total uncertainty factor of 10 was applied, including 3 to account for sensitive individuals and 3 for interspecies extrapolation. Use of greater factors would result in values similar to concentrations that would produce only mild irritation in human inhalation studies. Time scaling was performed using the equation  $C^n \times t = k$ , with the default values of n=1 and n=3 for extrapolation to longer and shorter durations, respectively.

**Additional toxicological information (including relevant results of a general literature search, if any)**

Toluene 2,4-diisocyanate is a corrosive substance, acting immediately at the point of contact. The degree of irritation seems to depend more on the exposure concentration, than the exposure-duration. Immediately after exposure, a decrease in respiratory rate can be detected in animals as well as humans. This rate becomes more graded after the initial exposure. Repeated exposure can induce asthmatic reactions in sensitized persons.

Sensitization with the risk to develop subsequent allergic reactions can occur from repeated exposure over a long period of time to relatively low concentrations or from at least one exposure at a high concentration. Therefore the sensitisation endpoint cannot be used for the derivation of intervention values. Substance is not reproductive toxic.

H315: Causes skin irritation; H317: May cause an allergic skin reaction; H319: Causes serious eye irritation; H330: Fatal if inhaled; H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled; H335: May cause respiratory irritation; H351: Suspected of causing cancer.

**Carcinogenicity and derivation of the CRP value**

IARC classification toluene diisocyanates: 2B (possibly carcinogenic to humans).

No carcinogenic risk potency (CRP) was derived.

Although carcinogenicity data for TDI are conflicting, it can be concluded that carcinogenicity is route-specific. The oral carcinogenicity may be due to the formation of toluene diamide (TDA) that is not formed after inhalation exposure. Based on the similar behaviour of TDA and 2,4-TDI, IARC has classified TDI in accordance with TDA. USEPA has not classified 2,4-TDI. For this inhalation scenario, CRP calculation is not applicable.

**Odour and derivation of the LOA value**

Odour: Pungent odour (sweet and fruity)

No LOA was derived due to lack of reliable data.

Direct odour recognition has been reported at 0.05 ppm (0.36 mg/m<sup>3</sup>) and above.

**Other standards and guidelines (1h values in mg/m<sup>3</sup>, unless otherwise indicated)<sup>a</sup>**

<b>VRW level</b> <b>0.15</b>	<b>AEGL-1</b> <b>0.14</b>	<b>ERPG-1</b> <b>0.07</b>	<b>IDLH: 18 (30 min)</b>
<b>AGW level</b> <b>0.60</b>	<b>AEGL-2</b> <b>0.59</b>	<b>ERPG-2</b> <b>1.09</b>	
<b>LBW level</b> <b>3.7</b>	<b>AEGL-3</b> <b>3.63</b>	<b>ERPG-3</b> <b>4.35</b>	

<sup>a</sup> Note that the AEGL and ERPG values as presented here (in mg/m<sup>3</sup>) are derived using the conversion factors of the AEGL and ERPG, respectively.