Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport

Stofdocument deel A

CAS-nr: 101-68-8

Difenylmethaan-4,4'-diisocyanaat

$C_{15}H_{10}N_2O_2$

VN-nr: 2206
GEVI: 60

Synoniemen: 4,4`-methyleendifenyldiisocyanaat, MDI, methyleen-bis(fenyl)isocyanaat
(Engels: methylene diphenyl diisocyanate)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m^3)**	0,20	0,20	0,20	0,20	0,20	0,20
Alarmeringsgrenswaarden	**AGW (mg/m^3)**	15	10	8,1	4,0	2,0	1,0
Levensbedreigende waarden	**LBW (mg/m^3)**	44	31	24	19	15	7,7

Datum vaststelling: 31-10-2017

1 mg/m^3 = 0,096 ppm; 1 ppm = 10,412 mg/m^3

Explosiegrens: 0,4 vol % .≈ 4000 ppm = 42000 mg/m^3

Geur: karakteristieke sinaasappelachtige geur

LOA: niet afgeleid

Fysisch-chemische eigenschappen

Uiterlijk: witte tot lichtgele schilfers of poeder; wordt donkerder bij blootstelling aan licht en lucht
Brand: moeilijk brandbaar. Bij vele reacties kans op brand en explosie.

Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,00

Molecuulmassa:	250,3 g/mol
Zuurgraad:	Geen data
LogKow:	4,5
Wateroplosbaarheid:	reactie
Verzadigde dampdruk:	<0,00002mbar

Overige informatie

Publieke grenswaarde:
geen
MAK: 0,05 mg/m^3
TLV-TWA: 0,052 mg/m^3

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder AGW:	irritatie aan ogen, neus en luchtwegen, keelpijn, hoesten, rhinitis, hoofdpijn, misselijkheid, piepende ademhaling
AGW → LBW:	ernstige luchtwegirritatie, onregelmatige ademhaling, benauwdheid, long oedeem
Boven LBW:	ademnood, sterfte

LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Difenylmethaan-4,4`-diisocyanaat is sterk irriterend voor de ogen en luchtwegen. Bij hoge concentraties werkt de stof bijtend.
- Bij inademing van hoge concentraties gaan vooral effecten op het alveolaire niveau overheersen, zoals longoedeem en Type IIA reacties
- Blootstelling kan een astmatische reactie veroorzaken.
- De stof is sensibiliserend. Na sensibilisatie kan de stof luchtwegallergie veroorzaken na inhalatie of huidallergie bij dermaal contact. Kruisgevoeligheid met andere diisocyanaten is mogelijk.

Effecten bij blootstelling aan vloeistof/vaste stof
(smeltpunt van deze vaste stof rond 40 °C)
Huidcontact: roodheid en pijn, blaren
Oogcontact: roodheid en pijn

Carcinogeniteit
IARC classificatie: 3
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp
algemeen: frisse lucht, rust, halfzittende houding en onmiddellijk arts raadplegen.

Ontsmetting vloeistof
huid: overmaat stof opdeppen, verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen..
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.
inslikken: mond laten spoelen (uitspugen!), en onmiddellijk arts raadplegen.

Specifieke behandeling en materialen*: geen*.
Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor informatie met betrekking tot medisch handelen

National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

Stofdocument deel B

CAS-nr: 101-68-8 **methylene diphenyl diisocyanate** **$C_{15}H_{10}N_2O_2$** **UN-nr: 2206**

Basis for the Dutch Intervention Values

VRW: Based on information as described in ERPG-document, but in contrast to ERPG values are derived for all time-points.

AGW: Based on information as described in ERPG-document, different values are derived, other time-points added

LBW: Based on information as described in ERPG-document, different values are derived, other time-points added

Date: 31-10-2017 ERPG 2011

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	0.20	0.20	0.20	0.20	0.20	0.20	Erythema and restlessness in rats
AGW	15	10	8.1	4.0	2.0	1.0	Ocular and respiratory irritation in rats
LBW	44	31	24	19	15	7.7	Rat lethality data (4 hr LC_{01})

Derivation of the Dutch Intervention Values

VRW: In a 1-hour acute inhalation toxicity study male rats (6/group) were exposed to 0.6, 80.8, 162, 171.5, 186.6, 562.5 or 1530 mg/m^3 MDI. Clinical signs observed at 80.8 mg/m^3 were salivation, lacrimation, nasal drip, nasal porphyrin discharge, dyspnea and escape behaviour. Clinical signs at 0.6 mg/m^3 in the same study consisted of slight erythema and restlessness. This study was designed as an acute lethality study with a reported LC_{50} of 178 mg/m^3. The effects observed at the next lowest level do not meet the criteria for AGW effects. The effects (erythema and restlessness) at 0.6 mg/m^3 were considered VRW effects and this level was used as point of departure. An overall uncertainty factor of 3, instead of 3x3, was considered sufficient to account for inter- and intraspecies differences, because of the large dose-spacing between the NOAEL and LOAEL. Timescaling was not applied as local effects are considered to be concentration-dependent rather than time-dependent.

AGW: In a 1-hour acute inhalation toxicity study male rats (6/group) were exposed to 0.6, 80.8, 162, 171.5, 186.6, 562.5 or 1530 mg/m^3 MDI. Clinical signs observed at 80.8 mg/m^3 were salivation, lacrimation, nasal drip, nasal porphyrin discharge, dyspnea and escape behaviour. Clinical signs at 0.6 mg/m^3 in the same study consisted of slight erythema and restlessness. This study was designed as an acute lethality study with a reported LC_{50} of 178 mg/m^3. The effects observed at the lowest level do not meet the criteria for AGW effects. The effects (reversible excessive lacrimation) at 80.8 mg/m^3 are slightly above the threshold for AGW effects and very near the threshold for lethality in this study. However, this level was considered to be most suitable as point of departure for derivation of the AGW. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n = 3, to calculate to longer and shorter durations, respectively.

LBW: Two acute inhalation studies were performed in rats with methylene diphenyl diisocyanate (MDI) in monomeric form for 4 and 1 hour(s) in various concentrations. As the 1 hour exposure study (see AGW for description) resulted in LC_{01} and LC_{50} values unrealistically close to each other this study was not further considered for LWB derivation. In the 4 hour exposure study (a non-published report by Bayer, 2008) Wistar rats (5/sex/concentration) were exposed nose only to aerosolized concentrations of MDI (MMAD of <3 µm) at gravimetrical concentrations of 300, 354.2, 399.2, 500 and 553.8 mg/m^3 for 4 hours. At 300 mg/m^3 no animals died. Lethality was observed from 354.2 mg/m^3 onwards: 2/10, 7/10, 3/10, 8/10 animals died at the respective concentration levels for both sexes combined. The reported LC_{50} and LC_{01} were 413 and 139 mg/m^3, respectively. With DoseResp a 4h LC_{01}-value of 153 mg/m^3 was calculated. This value is used as point of departure for LBW derivation. The default uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time scaling was performed using the equation $C^n \times t = k$ with the default n = 1 and n = 3, to calculate to longer and shorter durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)
The substance is a solid with a low vapour pressure. Inhalation exposure will occur via aerosols. Methylene diphenyl 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. The substance has sensitizing properties. Methylene diphenyl diisocyanate is not a developmental or reproductive toxicant. H315: Causes skin irritation; H317: May cause an allergic skin reaction; H319: Causes serious eye irritation; H332: Harmful if inhaled; H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled; H335: May cause respiratory irritation; H351: Suspected of causing cancer; H373: May cause damage to the organs through prolonged or repeated exposure.

Carcinogenicity and derivation of the CRP value
IARC classification: 3 (not classifiable as to its carcinogenicity to humans) No carcinogenic risk potency (CRP) was derived.

Odour and derivation of the LOA value
Odour: orange-like odour According to the ERPG, 2010 odour threshold levels of 2-4 mg/m^3 have been reported. No LOA was derived due to the absence of reviewed data.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)[a]

VRW level	*AEGL-1*	*ERPG-1*		*IDLH:* 75 mg/m^3 (30 minutes)
0.20	-	NA		
AGW level	*AEGL-2*	*ERPG-2*		
8.1	-	5		
LBW level	*AEGL-3*	*ERPG-3*		
24	-	55		

[a] Note that the ERPG values as presented here (in mg/m^3) are derived using the conversion factors of the ERPG.