

## Stofdocument deel A

CAS-nr: 106-93-4

**Ethyleendibromide**

BrCH<sub>2</sub>CH<sub>2</sub>Br

VN-nr: 1605

GEVI: 66

**Synoniemen:** 1,2-dibroomethaan, EDB (Engels: ethylene dibromide)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	<b>VRW (mg/m<sup>3</sup>)</b>	65	65	65	65	65	NA
Alarmeringsgrenswaarden	<b>AGW (mg/m<sup>3</sup>)</b>	970	430	260	150	93	56
Levensbedreigende waarden	<b>LBW (mg/m<sup>3</sup>)</b>	2900	1300	770	460	280	170
Datum vaststelling: 06-10-2016		1 mg/m <sup>3</sup> = 0,128 ppm; 1 ppm = 7,82 mg/m <sup>3</sup>					
<b>Explosiegrens:</b> geen data			<b>Geur:</b> scherp, zoete, chloroformachtige geur				
			<b>LOA:</b> 1.200 mg/m <sup>3</sup>				
Fysisch-chemische eigenschappen				Overige informatie			
<b>Uiterlijk:</b> kleurloze vloeistof		Molecuulmassa: 187,9 g/mol		Publieke grenswaarde:			
<b>Brand:</b> niet brandbaar		Zuurgraad: geen data		0,002 mg/m <sup>3</sup>			
		LogKow: 1,9		MAK: niet afgeleid			
<b>Relatieve dichtheid van verzadigd damp-lucht mengsel:</b> 1,08		Wateroplosbaarheid: 0,4 g/100 ml (slecht)		TLV-TWA: niet afgeleid			
		Verzadigde dampdruk: 15 mbar					
Toxicologische eigenschappen							
<b>Effecten bij inhalatoire blootstelling</b>				<b>Toxiciteit bij eenmalige, inhalatoire blootstelling</b>			
<u>Onder AGW:</u> lichte irritatie van ogen en neus				<ul style="list-style-type: none"> <li>De stof werkt irriterend op de ogen, de huid en de luchtwegen.</li> <li>Blootstelling aan (zeer hoge concentraties) ethyleendibromide kan longoedeem en chemische pneumonitis veroorzaken.</li> <li>De stof kan inwerken op de lever, de nieren en het centrale zenuwstelsel met als gevolg functiestoornissen en orgaanschade.</li> </ul>			
<u>AGW → LBW:</u> irritatie van de luchtwegen, misselijkheid, braken, duizeligheid, diarree, ademhalingsdepressie, sufheid							
<u>Boven LBW:</u> longontsteking en -oedeem, lever- en nierschade, coma en sterfte							
<i>LET OP: de afwezigheid van een VRW waarde betekent niet dat blootstelling onder de AGW zonder effecten is.</i>							
<b>Effecten bij blootstelling aan vloeistof</b>				<b>Carcinogeniteit</b>			
<i>Huidcontact:</i> roodheid en pijn. De stof wordt door de huid opgenomen!				IARC classificatie: 2A			
<i>Oogcontact:</i> roodheid en pijn, (reversibele) hoornvliesbeschadiging				CRP: 37 mg/m <sup>3</sup>			
Beknorte medische informatie							
<b>Ontsmetting damp</b>							
<i>algemeen:</i> frisse lucht, rust, halfzittende houding en onmiddellijk arts raadplegen							
<i>ogen:</i> minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen.							
<b>Ontsmetting vloeistof</b>							
<i>huid:</i> verontreinigde kleding uittrekken, spoelen en wassen met water en zeep, arts raadplegen.							
<i>ogen:</i> zie hierboven.							
<i>inslikken:</i> mond laten spoelen (uitspugen!), GEEN braken opwekken, en direct spoedeisende medische hulp inzetten.							
<b>Specifieke behandeling en materialen:</b> geen.							
Neem contact op met het NVIC (Tel: +31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen							

## Stofdocument deel B

CAS-nr: 106-93-4

**Ethylene dibromide**

BrCH<sub>2</sub>CH<sub>2</sub>Br

UN-nr: 1605

### Basis for the Dutch Intervention Values

**VRW:** Different point of departure as AEGL, different uncertainty factors, 2h value added

**AGW:** Different point of departure as AEGL, 2h value added

**LBW:** Different point of departure as AEGL, different uncertainty factors, 2h value added

Date: 06-10-2016

AEGL document: interim, 2008

### 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>	65	65	65	65	65	NR	Neurotoxicity in monkeys
<b>AGW</b>	970	430	260	150	93	56	LBW-values divided by three
<b>LBW</b>	2900	1300	770	460	280	170	Threshold for lethality in rats

### Derivation of the Dutch Intervention Values

**VRW:** VRW levels were based on repeated exposure of monkeys to 50 ppm (391 mg/m<sup>3</sup>), 7 hours/day for 49 exposures in 70 days. Effects indicative of neurotoxicity was observed throughout the study where monkeys exposed similarly to 25 ppm (196 mg/m<sup>3</sup>) showed no effects. It is noted that the neurotoxic effects were already observed at the first day of exposure. A total uncertainty factor of 3 (see LBW rationale) was applied. The VRW was set equal for all time points because CNS-effects are generally concentration-dependent but not time-dependent. The 8h VRW was not recommended due to conflict with the AGW level.

**AGW:** Due to lack of suitable data consistent with AGW-level effects, the LBW values were divided by 3

**LBW:** The derivation of the LBW values was based on an acute inhalation study in rats in which rats were exposed to ethylene dibromide in concentrations ranging from 100 to 10000 ppm (782 – 78200 mg/m<sup>3</sup>) for exposure durations up to 16h. These data were analysed using Doseresp and the resulting LC<sub>01</sub> values were 8707, 3872, 2322, 1393, 835 and 501 mg/m<sup>3</sup> for 10 min, 30 min, 1 hour, 2 hour, 4 hour and 8 hour with an n-value of 1.4. An uncertainty factor of 1 is used for the interspecies sensitivity, because similar effects and mode of actions were shown for various species (rodents, non-human primates and humans). Furthermore, PBPK modeling indicates that rats exposed to ethylene dibromide take up about three times more of the substance than humans and rats produce about five times more active metabolites from the P450 pathway when exposed to the substance than humans do. Rats also were predicted to produce about 80 times more GST metabolites than humans. The toxic effects of inhaling 1,2-dibromoethane are similar in humans and rats indicating similar pharmacodynamics. The difference in metabolite production would overwhelm any difference in pharmacodynamics, therefore an uncertainty factor of 1 is justified for interspecies variability. The default uncertainty factor of 3 was considered sufficient to account for intraspecies differences. This default intraspecies factor of 3 will cover a variability in the human population of a factor 10. Therefore, there is no reason to deviate from the default intraspecies uncertainty factor of 3.

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

When ethylene dibromide is metabolized, two reactive metabolites are produced. The metabolites of the P450 pathway bind to protein and the metabolites of the GST-pathway bind to DNA. The DNA reactive metabolites are considered to be related to the genetic toxicity and carcinogenicity of ethylene dibromide. The protein reactive metabolites are considered to be related to the cytotoxicity. The formation of bromine during metabolism is considered to contribute to the acute toxicity of ethylene dibromide.

A study on reproductive toxicity shows that after exposure of male rats to a concentration of 89 ppm (696 mg/m<sup>3</sup>) of ethylene dibromide for 7h/day, 5 days/week for 10 weeks, moderate to severe atrophy of the testes, epididymis, prostate and seminal vesicles was observed. None of the males exposed to 89 ppm impregnated even one female rat. A total of 10/50 females died after exposure to 80 ppm for 7h/day, 5 days/week for 3 weeks and none had normal estrous cycles until 3-4 days postexposure. Only 8/20 females exposed to 80 ppm

mated, and all that mated became pregnant. Rats were not exposed after mating. The number of viable implants/dam in females exposed to 80 ppm was reduced by 30% compared with that of controls. The presence of general toxicity made it difficult to relate the observed reproductive effects to the ethylene dibromide exposure. In a developmental toxicity study in rats exposed to 80 ppm (626 mg/m<sup>3</sup>) 23 h/day during GD6-15 half of the pregnant dams died. The other half of the dams experienced early resorptions and fetal deaths.

H350: May cause cancer, H331: Toxic if inhaled, H311: Toxic in contact with skin, H301: Toxic if swallowed, H319: Causes serious eye irritation, H315: Causes skin irritation, H335: May cause respiratory irritation

<b>Carcinogenicity and derivation of the CRP value</b>
<p>IARC classification: 2A (probably carcinogenic to humans)</p> <p>Derivation of the carcinogenic risk potency (CRP): 10<sup>-4</sup> risk level after inhalation: 10<sup>-4</sup>/0.6 mg/m<sup>3</sup> = 1.67 x 10<sup>-4</sup> mg/m<sup>3</sup> [EPA, 2004] CRP = (10<sup>-4</sup> risk level * average life span in hours)/DRCF = (1.67 x 10<sup>-4</sup> mg/m<sup>3</sup>* 613,200) /2.8 =37 mg/m<sup>3</sup></p>

<b>Odour and derivation of the LOA value</b>
<p>Odour: pungent, sweetish, chloroform like odour Odour threshold: 78.2 mg/m<sup>3</sup> [Ruth, 1986] LOA = 11.8 * ODT * 1.33 = 1,227 mg/m<sup>3</sup> (The concentration <u>L</u> leading to distinct <u>O</u> odour <u>A</u>wareness (I=3) is calculated using the formula: I = 2.33 * log (C/ODT + 0.5). A correction factor of 1.33 is applied to this value) The LOA lies above all intervention values except for the 10 min AGW value, and 10 min and 30 min LBW value.</p>

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

<b>VRW level</b>	<b>AEGL-1</b>	<b>ERPG-1</b>	<b>IDLH: 782 (30 minutes)</b>
<b>65</b>	130	-	
<b>AGW level</b>	<b>AEGL-2</b>	<b>ERPG-2</b>	
<b>260</b>	190	-	
<b>LBW level</b>	<b>AEGL-3</b>	<b>ERPG-3</b>	
<b>770</b>	360	-	