

Stofdocument deel A

CAS-nr: 106-89-8

Epichloorhydrine

C₃H₅ClO

VN-nr: 2023

GEVI: 63

Synoniemen: 1-chloor-2,3-epoxypropaan, (2-chloormethyl)oxiraan, γ-chloorpropyleenoxide (Engels: epichlorohydrin)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	VRW (mg/m³)	22	22	22	22	NA	NA
Alarmeringsgrenswaarden	AGW (mg/m³)	67	46	37	29	23	17
Levensbedreigende waarden	LBW (mg/m³)	170	120	95	76	60	30

Datum vaststelling: November 2015

1 mg/m³ = 0,260 ppm; 1 ppm = 3,85 mg/m³

Explosiegrens: LEL= 2,3 vol% ≈ 89.000 mg/m³

Geur: zoet, scherp en chloroform-achtig

LOA: 240 mg/m³

Fysisch-chemische eigenschappen		Overige informatie
Uiterlijk: kleurloze vloeistof	Molecuulmassa: 92,5 g/mol	Publieke grenswaarde: 0,19 mg/m ³ (8 uur) MAK: 8 mg/m ³ TLV-TWA: 2 mg/m ³ (huid)
Brand: brandgevaarlijk	Zuurgraad: Geen data	
Relatieve dichtheid van verzadigd damp-lucht mengsel: 1,05	LogKow: 0,45	
	Wateroplosbaarheid: 6 g/100 ml (matig) (10°C)	
	Verzadigde dampdruk: 17 mbar	

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling	Toxiciteit bij eenmalige, inhalatoire blootstelling
<p><u>Onder VRW:</u> geen effecten</p> <p><u>VRW → AGW:</u> irritatie van slijmvliezen (met name ogen en neus), roodheid huid</p> <p><u>AGW → LBW:</u> effect op de ongeboren vrucht, matige tot ernstige irritatie van luchtwegen, speekselvloed, keelpijn, hoesten, benauwdheid, branderig gevoel op de borst, misselijkheid, hoofdpijn, lever- en nierfunctiestoornissen</p> <p><u>Boven LBW:</u> ademstilstand, longoedeem, sterfte</p>	<ul style="list-style-type: none"> Epichloorhydrine is een alkylenderend epoxide verbinding en bevat een uiterst reactieve oxiraanring. Blootstellingen kunnen primair resulteren in irritatie van de slijmvliezen (ogen, neus, keel) en de huid. Deze klachten kunnen zich pas enkele uren na blootstelling openbaren en enkele dagen aanhouden. De stof kan mogelijk ontwikkelingstoxiciteit en abortus veroorzaken, alsmede depressie van het CZS. Blootstelling aan epichloorhydrine kan longoedeem en chemische pneumonitis veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning. Herhaaldelijke of langdurige blootstelling kan huidsensibilisatie veroorzaken met als gevolg allergische contactdermatitis.

Effecten bij blootstelling aan vloeistof	Carcinogeniteit
<p><u>Huidcontact:</u> bijtend, irritatie, roodheid, pijn, brandwonden, blaren, zwelling</p> <p><u>Oogcontact:</u> bijtend, irritatie, roodheid, pijn, slecht zicht, brandwonden, permanent verlies gezichtsvermogen</p>	<p>IARC classificatie: 2A CRP: 18.250 mg/m³</p>

Beknopte medische informatie

<p>Ontsmetting damp <i>algemeen:</i> frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.</p> <p>Ontsmetting vloeistof <i>huid:</i> verontreinigde kleding uittrekken, minimaal 20 min. spoelen met veel water of douchen en direct spoedeisende medische hulp inzetten.</p> <p><i>ogen:</i> minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.</p> <p><i>inslikken:</i> mond laten spoelen (uitspugen!), GEEN braken opwekken en direct spoedeisende medische hulp inzetten.</p> <p>Specifieke behandeling en materialen: geen.</p> <p>Neem contact op met het NVIC (tel: +31 (0)30 –274 8888) voor informatie met betrekking tot medisch handelen.</p>

Stofdocument deel B

CAS-nr: 106-89-8

Epichlorohydrin C₃H₅ClO

UN-nr: 2023

Basis for the Dutch Intervention Values

VRW: Same point of departure than AEGL but using different uncertainty factors 2h value added;

AGW: Different point of departure and different value for n than AEGL values, 2 h value added;

LBW: Different point of departure and different value for n than AEGL values, 2 h value added.

Date: November 2015

AEGL document: Final, 2014

Dutch Intervention Values (mg/m³)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	22	22	22	22	NA	NA	Threshold for irritation in humans
AGW	67	46	37	29	23	17	NOAEL for developmental toxicity in rats
LBW	170	120	95	76	60	30	Threshold for lethality (LC ₀₁) in rats

Derivation of the Dutch Intervention Values

VRW: Irritation is the most sensitive effect experienced by humans exposed to low concentrations of epichlorohydrin, and this endpoint will therefore be used to derive VRW values. Four human subjects were exposed to epichlorohydrin at concentrations of 17, 68, and 136 ppm (65, 262, 524 mg/m³) for 2 minutes. Three subjects exposed to 68 ppm (262 mg/m³) of epichlorohydrin reported no irritating effect, and one reported irritation to the pharynx. Two subjects exposed to 136 ppm (524 mg/m³) reported a cooling sensation in the eyes and mouth and two reported irritation to the eyes or pharynx. The point-of-departure is 17 ppm (65 mg/m³) for a 2 minute exposure; this concentration and time is a no-effect level for irritation. The default uncertainty factor of 3 for intraspecies variability is applied. Time-scaling is not performed because the irritative effects are not expected to become more severe with increasing exposure duration at this concentration. The 4-h and 8-h VRW values are set to NA (not applicable), due to conflict with AGW-values.

AGW: Groups of five or six presumed pregnant female rats were exposed to epichlorohydrin vapour concentrations of 0, 25, 50 or 100 ppm (0, 96, 193 or 385 mg/m³) epichlorohydrin for 7 hours/day on gestation days 6-15 and killed on day 16. Maternal toxicity consisting of decreased weight gain, decreased intra-abdominal adipose tissue, decreased thymus size, and an increased incidence of pale liver was observed in the 50 and 100 ppm (193 and 385 mg/m³) exposure groups. Three out of six rats exposed to 100 ppm (385 mg/m³) had 100% resorptions, one had normal foetuses and two rats had no evidence of being pregnant (no implantation sites). These effects were not reported at the 50 ppm (193 mg/m³) exposure concentration or below. Since resorptions can be induced by a single exposure and therefore are considered as an appropriate endpoint for an AGW, the 7-hour 50 ppm (193 mg/m³) exposure level as a NOAEL for developmental toxicity in rats is chosen as point of departure. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation Cⁿxt=k, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. The approach deviates from the AEGL-2 derivation where the AEGL-2 levels were calculated by dividing the AEGL-3 levels by 3.

LBW: LBW values were based on a rat lethality study. In this study, groups of 20 male Wistar rats were exposed under dynamic conditions to atomized (aerosolized) epichlorohydrin in a mixture of alcohol and lutrol (1:1) at epichlorohydrin concentrations of 296, 638, 1038, or 1440 mg/m³, respectively for 4 hours and observed for 2 weeks. The concentrations of epichlorohydrin in the chamber atmospheres were determined spectrophotometrically on air samples reacted with hydroxylamine. The number of deaths and time to death were concentration related. Using DoseResp the 4h LC₀₁ value was calculated which was used as point of departure for deriving the LBW values. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Time-scaling was performed using the equation Cⁿxt=k, using the default values for n of 1 and 3 for extrapolation to longer and shorter exposure durations, respectively. The LC₀₁ values were 1731, 1200, 952, 756, 600 and 300 mg/m³ for 10 min, 30 min, 1h, 2h, 4h and 8h exposure duration respectively. This approach deviates from the AEGL-3 derivation. AEGL-3 levels were based on two rat studies. A 1h study was used to derive the 10 min, 30 min and 1h AEGL-3 values. A 6h study was used to derive the 4h and 8h AEGL-3 value. Time-scaling was done by applying an n-value

of 0.87 which was based on rat LC₅₀ values for 1-, 4-, 6-, and 8-hour exposure derived from other studies.

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

The mechanism by which epichlorohydrin exerts its toxic effects is not known. Epichlorohydrin is a direct alkylating agent, which may account for some of its irritant properties.

Occupational exposure to epichlorohydrin did not reveal developmental or reproductive effects in human males as determined by sperm count and various hormone levels. A range finding study in rats using a concentration of 0, 25, 50 or 100 ppm (0, 96, 192 or 385 mg/m³) epichlorohydrin for 7 hours/day on gestation days 6-15, revealed maternal toxicity and effects of epichlorohydrin on resorptions (3/6 rats had 100% resorptions). These effects were used as POD for AGW.

H350: May cause cancer. H301/311/331: Toxic by inhalation, in contact with skin and if swallowed. H314: Causes burns. H317: May cause sensitisation by skin contact.

Carcinogenicity and derivation of the CRP value

IARC classification: 2A (probably carcinogenic to humans)

Derivation of the carcinogenic risk potency (CRP):

10⁻⁴ risk level after inhalation: 8.33 * 10⁻² mg/m³

CRP = (10⁻⁴ risk level * average life span in hours)/DRCF
= 8.33 * 10⁻² mg/m³ * 613.200 / 2.8 = 18,243 mg/m³

A cohort study of workers in the USA showed slight excesses of lung cancer. Another cohort in Europe was inconclusive. Carcinogenicity studies in rats showed that 30, 6-hour exposures (5 days/week) to 100 ppm of epichlorohydrin vapour followed by lifetime observation was very effective in inducing squamous cell carcinomas in the nasal cavity of rats. Whereas lifetime exposure to 30 ppm (6 hours/day, 5 days/week) was almost ineffective. This study demonstrated that short-term high level exposures are more effective than long-term low-level exposures for nasal tumour induction.

Odour and derivation of the LOA value

Odour: sweet, pungent or chloroform-like

OT₅₀: 15 mg/m³ [Shell Oil 1992 & Van Doorn 2002] adjusted by [Ruijten et al., 2009]

LOA = 11.8 * OT₅₀ * 1.33 = 240 mg/m³

(The concentration level leading to distinct odour awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT₅₀) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies above the VRW and AGW at all time points. It is lower than the LBW levels at the 10, 30, 60 and 120 minutes time points and higher than the other LBW time points.

Other standards and guidelines (1h values in mg/m³, unless otherwise indicated)

VRW level 22	AEGL-1 6.5	ERPG-1 19	IDLH: 290 mg/m³ (30 minutes)
AGW level 37	AEGL-2 92	ERPG-2 77	
LBW level 95	AEGL-3 280	ERPG-3 390	