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

Stofdocument deel A

CAS-nr: 74-83-9 **Methylbromide** **CH_3Br** **VN-nr: 1062**

GEVI: 26

Synoniemen: broommethaan, monobroommethaan (Engels: methyl bromide)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m^3)**	NA	NA	NA	NA	NA	NA
Alarmeringsgrenswaarden	**AGW (mg/m^3)**	3700	1500	840	470	260	260
Levensbedreigende waarden	**LBW (mg/m^3)**	13.000	5200	2900	1600	920	520

Datum vaststelling: 24-09-2009

1 mg/m^3 = 0,253 ppm; 1 ppm = 3,95 mg/m^3

Explosiegrens: LEL = 10 vol% ≈ 400.000 mg/m^3

Geur: vrijwel geen geur; geur is beschreven als zoet en chloroformachtig, fruitig

LOA: 1240 mg/m^3

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos gas

Brand: moeilijk brandbaar

Relatieve dichtheid gas: 3,3

Molecuulmassa: 95 g/mol
Zuurgraad: geen data
LogKow: geen data
Wateroplosbaarheid: 1,5 g/100 ml (matig)
Verzadigde dampdruk: 1900 mbar

Overige informatie

Publieke grenswaarde: niet afgeleid
MAK: 4,0 mg/m^3
TLV-TWA: 4,0 mg/m^3 (huid)

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

*Onder **AGW***: geen informatie

AGW → LBW: keelpijn, hoesten, misselijkheid, braken, hoofdpijn, duizeligheid, zwaktegevoel, lever- en nierschade, benauwdheid, longoedeem, hartritmestoornissen

Boven LBW: convulsies, coma, sterfte

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

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Methylbromide is veroorzaakt effecten op het CZS en de luchtwegen.
- Methylbromide kan longoedeem veroorzaken. De verschijnselen hiervan kunnen vertraagd optreden en versterkt worden door lichamelijke inspanning.
- Methylbromide kan lever- en nierschade veroorzaken.
- Bij blootstelling aan lage concentraties kunnen de effecten vertraagd optreden.

Effecten bij blootstelling aan vloeistof

Huidcontact: bij bevriezing: ernstige bevriezingsverschijnselen zoals pijn, blaren en wonden

Oogcontact: bij bevriezing: pijn ernstige brandwonden

Carcinogeniteit

IARC classificatie: 3
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting gas

algemeen: frisse lucht, GEEN mond-op-mondbeademing, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.

Ontsmetting vloeistof

huid: aan de huid vastgevroren kleding NIET lostrekken, minimaal 20 min. spoelen met veel water of douchen en ONMIDDELLIJK arts raadplegen..

ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

inslikken: n.v.t. (gas)

Specifieke behandeling en materialen

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: 74-83-9 **Methyl bromide** CH_3Br **UN-nr: 1062**

Basis for the Dutch Intervention Values

VRW: AEGL value is adopted, 2h value added

AGW: AEGL value is adopted, 2h value added

LBW: AEGL value is adopted, 2h value added

Date: 24-09-2009 | AEGL document: Final, 2012

Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	NR	NR	NR	NR	NR	NR	Not recommended due to insufficient data
AGW	3700	1500	840	470	260	260	Threshold of neurotoxic effects
LBW	13,000	5200	2900	1600	920	520	Threshold of lethality in animals

Derivation of the Dutch Intervention Values

VRW: Because methyl bromide is not detectable by sensory irritation at concentrations below the AGW, a VRW was not derived.

AGW: For methyl bromide, the endpoint of neurotoxicity, leading to an inability to escape is the most relevant endpoint for the AGW. Because of the steep dose-response curve for such effects, a NOAEL for neurotoxicity is the appropriate endpoint for the AGW. Studies with the dog and rat (the mouse was considered unusually sensitive due to its high tissue levels of the liver enzyme GST) indicate that 200 ppm (790 mg/m^3) for 4 hours is a NOAEL for clinical signs indicative of neurotoxicity. Because uptake of methyl bromide is greater in rodents than in humans (based on comparative respiratory rates and comparisons with methyl chloride) and because GST levels in rodents are higher than in humans, resulting in more rapid production of toxic metabolites, an interspecies uncertainty factor of 1 was applied. Humans differ in their capacity to metabolize methyl bromide, but, toxicologically, the difference is considered to be less than 3-fold. An intraspecies uncertainty factor of 3 was applied. The resulting 4-hour value of 67 ppm (260 mg/m^3) was time scaled to the other exposure durations using $C^n \times t = k$ and an n value of 1.2 (based on lethality data in the rat). Because the time scaled 8-hour value of 37 ppm (150 mg/m^3) is close to the chronic NOAEL of 33 ppm (130 mg/m^3) for mice and less than the 5-day NOAEL of 55 ppm (220 mg/m^3) for clinical signs and tissue lesions in dogs and 36-week NOAEL of 55 ppm (220 mg/m^3) for neurobehavioral parameters and nerve conduction velocity in rats, this is considered as a too high value. Therefore, the 8-hour value was set equal to the 4-hour value.

LBW: The LBW values were based on the $BMCL_{05}$ of 701 ppm (2770 mg/m^3) in a 4-hour exposure of rats. This value (701 ppm, 2770 mg/m^3) was also the highest nonlethal value in the study. The 4-hour 701 ppm (2770 mg/m^3) concentration was adjusted by inter and intraspecies uncertainty factors of 1 and 3, respectively as for the AGW above, and time scaled using $C^{1.2} \times t = k$, based on lethality data in the rat. The 8-hour LBW value of 520 mg/m^3 is supported by repeat-dose studies in which dogs exposed to 156 or 158 ppm (616 or 624 mg/m^3) for 7 hours/day did not exhibit severe clinical signs until the second or third day of exposure. There were no remarkable histopathological lesions in the dogs at autopsy following a 4-day exposure, but cerebellar lesions were observed following 6 days of exposure to 158 ppm (624 mg/m^3).

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

Inter-individual variation in the rate of metabolism of methyl halides has been observed in humans. At least two distinct populations of humans with differences in the rate of metabolism of the structurally-similar methyl chloride have been identified. Fast metabolism may lead to the formation of toxic metabolites that can exert their action before they can be eliminated whereas slow metabolizers would be expected to be less susceptible to the toxic effects of methyl halides. For the related chemical, methyl chloride, uptake while

inhaling 50 ppm differed less than 3-fold among slow and fast metabolizers. Elimination was rapid by both groups following termination of the exposure. Elimination was more rapid by those volunteers with the lower blood and expired air concentrations. The authors explained the difference in the two groups by a two-fold difference in the rate at which they metabolized methyl chloride. They considered the difference of questionable toxicological significance. In general, populations that have kidney or liver disease, anemia, or neurological deficits may be more susceptible to the toxic effects of methyl chloride.

Methyl bromide has been responsible for many occupational poisoning incidents, reflecting its wide use as a fumigant. Although many occupational and accidental exposures to methyl bromide have occurred, few cases accurately document exposure concentrations or durations. Methyl bromide is practically odourless, even at lethal concentrations. Descriptive symptoms indicate methyl bromide acts on the central nervous system (headache, visual disturbance, mental disturbance, nausea, vomiting, etc.) and directly on the lungs (lung edema).

Studies with rats and rabbits indicate that inhalation exposure up to 70 ppm (280 mg/m^3) during gestation does not result in any significant developmental effects.

H301: Toxic if swallowed; H315: Causes skin irritation; H319: causes serious eye irritation; H331: Toxic if inhaled; H335: May cause respiratory irritation; H341: Suspected of causing genetic defects; H373: May cause damage to organs.

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.

Methyl bromide tested positive in numerous mutagenicity and genotoxicity tests. Mutagenicity did not require metabolic activation which is consistent with the direct-acting alkylation of DNA. Alkylation suggests that methyl bromide may be carcinogenic, but carcinogenicity has not been established following chronic studies with rats and mice.

Odour and derivation of the LOA value

Odour: Methyl bromide is practically odourless, even at lethal concentrations. Reported odour thresholds are variable: 20-1000 ppm (79-4000 mg/m^3). The odour has been described as sweetish and chloroform-like, but additional descriptions include musty or fruity at concentrations above 1000 ppm (4000 mg/m^3) or faintly acrid at around 500 ppm (2000 mg/m^3).

Using the lowest odour threshold to derive the LOA would provide,

LOA = 11.8 * 79 * 1.33 = 1240 mg/m^3

(The concentration Level leading to distinct Odour Awareness (I=3) is calculated using the formula: $I = 2.33 * \log (C/OT_{50}) + 0.5$. A correction factor of 1.33 is applied to this value)

The LOA lies in the range of the AGW and LBW.

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

VRW level **NR**	*AEGL-1* NR	*ERPG-1* NR		*IDLH:* 990 (30 min)
AGW level **840**	*AEGL-2* 830	*ERPG-2* 200		
LBW level **2900**	*AEGL-3* 2900	*ERPG-3* 790		