The MAK Collection for Occupational Health and Safety

Methyl vinyl ether

MAK Value Documentation, addendum – Translation of the German version from 2018

A. Hartwig[1,*], MAK Commission[2,*]

1 *Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Institute of Applied Biosciences, Department of Food Chemistry and Toxicology, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany*

2 *Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany*

***** *email: A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)*

Keywords: methyl vinyl ether; MAK value; maximum workplace concentration; peak limitation; developmental toxicity; toxicity; olfactory epithelium

Citation Note: Hartwig A, MAK Commission. Methyl vinyl ether. MAK Value Documentation, addendum – Translation of the German version from 2018. MAK Collect Occup Health Saf [Original edition. Weinheim: Wiley-VCH; 2018 Oct;3(4):1923-1931]. Corrected republication without content-related editing. Düsseldorf: German Medical Science; 2025. https://doi.org/10.34865/mb10725e6418_w

Republished (online): 12 Dec 2025

Originally published by Wiley-VCH Verlag GmbH & Co. KGaA; https://doi.org/10.1002/3527600418.mb10725e6418

Addendum completed: 05 Apr 2017

Published (online): 19 Oct 2018

The commission established rules and measures to avoid conflicts of interest.

Methyl vinyl ether

MAK Value Documentation

A. Hartwig[1,*], MAK Commission[2,*]

DOI: 10.1002/3527600418.mb10725e6418

Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has re-evaluated the maximum concentration at the workplace (MAK value) and the Pregnancy Risk Group of methyl vinyl ether [107-25-5].

There are no new data. Methyl vinyl ether was assessed in two 28 day inhalation studies, the first with 5 male and 5 female rats each and concentrations of 0, 500, 3500, 25 000 ml/m³ and a second with 10 male rats each and concentrations of 0, 150, 500, 1500 ml/m³. In the first study 3500 ml/m³ was the systemic NOAEC for females and local NOAEC for males and females. In male rats, changes in haematological and clinico-chemical parameters were observed in all exposure groups independent of the concentration. These effects could not be reproduced in the second study. At 3500 ml/m³ the body weight gains of male rats were reduced. This reduction was not seen in the second study with a higher number of animals. Therefore the commission now evaluates the effects at 3500 ml/m³ as incidental, maybe due to the lower number of animals, and defined 3500 ml/m³ as NOAEC. As the margin of the MAK value of 200 ml/m³ to slight effects at 25 000 ml/m³ is large enough it also accounts for the increased respiratory volume at the workplace (the blood:air partition coefficient of methyl vinyl ether is > 5; see List of MAK- and BAT Values, Sections I b and I c). Therefore the MAK value of 200 ml/m³ is confirmed.

Since a systemic effect is critical, Peak Limitation Category II is retained. No data concerning half-life are available; therefore the default excursion factor of 2 is confirmed.

For rats, the NOAEC for developmental toxicity after inhalation is 5000 ml methyl vinyl ether/m³, at 10 000 ml/m³ variations and retarded ossification were observed. Even considering the increased respiratory volume at the workplace the difference of the NOAEC for developmental toxicity to the MAK value is sufficient so that methyl vinyl ether remains assigned to Pregnancy Risk Group C.

Keywords

methyl vinyl ether; toxicokinetics; metabolism; (sub)acute toxicity; (sub)chronic toxicity; reproductive toxicity; peak limitation; prenatal toxicity; occupational exposure; maximum workplace concentration; MAK value; toxicity; hazardous substance

Author Information

[1] Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Department of Food Chemistry and Toxicology, Institute of Applied Biosciences, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany

[2] Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany

[*] Email: A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)

1924

Methyl vinyl ether

[107-25-5]

Supplement 2018

MAK value (2011)	**200 ml/m³ (ppm) ≙ 482 mg/m³**
Peak limitation (2011)	**Category II, excursion factor 2**
Absorption through the skin	**–**
Sensitization	**–**
Carcinogenicity	**–**
Prenatal toxicity (2011)	**Pregnancy Risk Group C**
Germ cell mutagenicity	**–**
BAT value	**–**
Vapour pressure at 20 °C	1756 hPa (SRC 2011)
log K_{OW}[1)]	0.422 (SRC 2011)
1 ml/m³ (ppm) ≙ 2.409 mg/m³	**1 mg/m³ ≙ 0.415 ml/m³ (ppm)**

Documentation for methyl vinyl ether was published in 2012 (documentation "Methylvinylether" 2012, available in German only).

In 2016, the Commission began using a revised approach for assessing substances with a MAK value based on systemic effects and derived from inhalation studies in animals or studies with volunteers at rest; this new approach takes into account that the respiratory volume at the workplace is higher than under experimental conditions. This applies to gases or vapour with a blood:air partition coefficient > 5 (see List of MAK and BAT Values, Sections I b and I c). A value of 1184 is calculated for methyl vinyl ether based on the above given data for vapour pressure and log K_{OW} and using the formula of Buist et al. (2012). This supplement evaluates whether the MAK value and the pregnancy risk group for methyl vinyl ether need to be re-assessed as a result of the higher respiratory volume at the workplace.

1) octanol/water partition coefficient.

Toxicokinetics and metabolism

There are no new data available.

The documentation published in 2012 (documentation "Methylvinylether" 2012, available in German only) reported a maximum uptake of 12.9 mg/kg body weight and hour for rats via inhalation; uptake via inhalation is saturable (see Figure 3 in Andersen et al. 1980). About 75% of the maximum uptake is reached at 1500 ml/m^3.

There are no studies that investigate metabolism of the substance. In the case of isobutyl vinyl ether, a decrease in pH increases the rate of hydrolysis, and so it can be assumed that in the case of methyl vinyl ether, hydrolysis to acetaldehyde takes place in the acidic nasal epithelium or stomach. No experimental studies have been carried out.

Subacute, subchronic and chronic toxicity

Inhalation

There are no new data available.

The documentation published in 2012 (documentation "Methylvinylether" 2012, available in German only) included two 28-day inhalation studies carried out according to OECD Test Guideline 412: one study investigated groups of 5 male and 5 female Wistar rats exposed to methyl vinyl ether concentrations of 0, 500, 3500 and 25 000 ml/m^3 (BG Chemie 1989 a, c), and another clarified questionable findings from the first study concerning the effects on male rats. Groups of 10 male Wistar rats were exposed in this study to methyl vinyl ether concentrations of 0, 150, 500 and 1500 ml/m^3 (see Table 1; BG Chemie 1989 b, c). In the first study, reduced body weight gains, increased clotting time, and a decrease in the lymphocyte count and total protein were observed in males at 500 ml/m^3 and above. A reduction in absolute spleen and lung weights was reported, but there was no change in the relative organ weights. For this reason, it is quite likely that the reduction in absolute organ weights was caused by the lower body weights. The haematological and clinico-chemical findings were not dependent on the concentration (see Table 1). Each of these parameters was already increased or decreased at 500 ml/m^3 and maintained this level up to the exposure concentration of 25 000 ml/m^3 (plateau concentration). Similar haematological and clinico-chemical findings were not observed in the females, even at 25 000 ml/m^3. Reduced body weights, increased relative liver weights and a decrease in the number of olfactory epithelial cells were observed at this concentration. The 18% increase in relative liver weights recorded in females has no histopathological correlate and, in the opinion of the Commission, is not yet adverse. This means that not significantly reduced body weights and not significantly reduced body weight gains were the only systemic effects observed in females at 25 000 ml/m^3. Therefore, a systemic and local NOAEC (no observed adverse effect concentration) of 3500 ml/m^3 was derived for methyl vinyl ether from the effects observed in female rats in the first study, whereas no NOAEC was determined for male rats.

In the second study, with exposure of 10 male Wistar rats per concentration group, no effects on behaviour, body weights, organs, and haematological or clinico-chemical parameters, and no histopathological findings in the organs and tissues prescribed by OECD Test Guideline 412 were observed. An additional examination of the bone marrow did not reveal any effects caused by the substance. As the study examined twice as many male animals and focused on the findings of the first study, without being able to reproduce them, this calls the findings in male rats from the first study into question. The highest concentration of methyl vinyl ether tested of 1500 ml/m³ is thus the local and systemic NOAEC of this study. This was the value that was used to derive the MAK value in 2012.

In the first study, both body weights and body weight gains were significantly decreased in the males at 3500 ml/m³ and above. However, it needs to be taken into consideration that in the first study, the body weights of the animals in the two high concentration groups were 7% lower at the beginning of exposure than those of the control animals. For this reason, only the effect on body weight gains can be assessed. However, the effect of methyl vinyl ether on body weight gains in males is contradictory and questionable because in the first study, the body weight gains attained merely 85% of the level of those in the control animals at 500 ml/m³, but were not decreased in the second study in comparison with those in the controls, even at a concentration of 1500 ml/m³. A possible explanation might be that, in addition to the better randomization of the animals in the second study, 10 male animals were used per concentration group. The findings of the second study would thus be less affected by extreme individual body weights than would be the case in the first study with only 5 animals per group.

The findings from the second study have greater relevance for males. Additional parameters were investigated and twice as many animals tested. Furthermore, the study specifically focused on the findings from the first study, but was not able to reproduce them. Because of the questionable effect on body weights observed in the first study, 3500 ml/m³ has now been established as the NOAEC for all the effects of methyl vinyl ether in male animals.

Developmental toxicity

There are no new data available.

The documentation published in 2012 (documentation "Methylvinylether" 2012, available in German only) included a study of the toxic effects on development of methyl vinyl ether carried out in Wistar rats according to OECD Test Guideline 414. The study yielded a NOAEC of 5000 ml/m³ for the embryotoxic effects of methyl vinyl ether and described delayed ossification and minor variations at methyl vinyl ether concentrations of 10 000 ml/m³. Up to 19 500 ml/m³ maternal toxicity was slight and was detected on day 21 of gestation in the form of slightly reduced body weight gains at 5000 and 19 500 ml/m³, but not at 10 000 ml/m³.

Table 1 Findings on day 28 after 4-week exposure (6 hours/day, 5 days/week) of Wistar rats to methyl vinyl ether (BG Chemie 1989 a, b, c)

Study parameters		Exposure concentration			
Study 1: **5 ♂, 5 ♀**		**0 ml/m³**	**500 ml/m³**	**3500 ml/m³**	**25 000 ml/m³**
initial body weight [g]	♂	181	176	167	169
	♀	142	143	143	144
body weight at end of study [g]; AV ± SD	♂	272 ± 11.0	253 (93%) ± 5.1	233* (86%) ± 12.2	217** (79%) ± 8.8
	♀	171 ± 4.2	172 (100%) ± 6.4	168 (98%) ± 7.4	162 (95%) ± 2.7 significantly* reduced only in week 3
increase in body weight [g]; AV	♂	91	77 (85%)	65* (71%) significantly reduced only in week 1	48** (53%) significantly reduced in all weeks
	♀	28	29 (104%)	25 (89%)	18 (64%)
prothrombin time [sec]; AV ± SD	♂	41.1 ± 0.9	46.0 ± 2.7	46.5 ± 0.6	46.2 ± 1.6
	♀	39.3 ± 0.9	39.5 ± 1.3	39.8 ± 1.5	42.7 ± 1.1
reticulocytes (‰); AV ± SD	♂	24.4 ± 2.8	16.4 ± 2.4	16.0 ± 3.2	13.2 ± 3.4
	♀	7.2 ± 0.5	8.0 ± 1.8	8.4 ± 2.1	11.6 ± 2.4
white blood cells ($x10^{-9}$/l); AV ± SD	♂	16.5 ± 1.5	11.4 ± 0.6**	12.2 ± 1.1*	13.1 ± 0.1
	♀	9.8 ± 0.9	9.0 ± 0.5	10.2 ± 1.1	8.9 ± 0.6
lymphocytes ($x10^{-9}$/l)	♂	15.8 ± 1.5	10.4 (66%) ± 0.5**	11.3 (71%) ± 0.9*	11.9 (75%) ± 1.0*
	♀	8.0 ± 1.0	8.2 ± 0.6	8.7 ± 1.1	7.8 ± 0.5
relative fraction; SD	♂	95.2% ± 0.6	91.2% ± 1.8	93.0% ± 0.6	90.8% ± 3.3
	♀	81.2% ± 3.2	91.0% ± 1.9	84.6% ± 2.8	87.6% ± 2.1

Table 1 (continued)

Study parameters		Exposure concentration			
total protein [g/l]; AV ± SD	♂	56.7 ± 0.5	53.8 ± 0.3**	53.4 ± 0.2**	52.5 ± 0.8**
	♀	54.1 ± 0.8	53.5 ± 1.2	51.5 ± 1.3	54.5 ± 0.5
AST [U/l]; AV ± SD	♂	60.3 ± 2.0	58.9 ± 2.5	59.0 ± 1.6	51.1 ± 0.7**
	♀	70.1 ± 1.1	67.3 ± 2.2	70.4 ± 3.4	63.4 ± 2.7
Organ weights					
spleen abs. [g]; AV ± SD	♂	0.505 ± 0.027	0.450 (89%) ± 0.008	0.437 (86%) ± 0.015*	0.384 (76%) ± 0.014**
	♀	0.419 ± 0.040	0.374 (89%) ± 0.015	0.352 (84%) ± 0.013	0.310 (74%) ± 0.018*
rel. [g/kg body weight]; AV ± SD	♂	1.86 ± 0.07	1.78 ± 0.03	1.90 ± 0.13	1.77 ± 0.06
	♀	2.45 ± 0.21	2.18 ± 0.08	2.10 ± 0.04	1.91 ± 0.1
lungs abs. [g]; AV ± SD	♂	1.46 ± 0.07	1.42 (97%) ± 0.07	1.22 (83%) ± 0.03*	1.18 (81%) ± 0.04*
	♀	1.11 ± 0.05	1.04 (94%) ± 0.03	1.05 (95%) ± 0.03	1.07 (96%) ± 0.04
rel. [g/kg body weight]; AV ± SD	♂	5.35 ± 0.07	5.61 ± 0.31	5.27 ± 0.19	5.47 ± 0.24
	♀	6.49 ± 0.18	6.04 ± 0.15	6.26 ± 0.09	6.59 ± 0.16
liver rel. [g/kg body weight]; AV ± SD	♂	41.2 ± 1.0	42.3 ± 0.9	41.2 ± 1.0	44.8 ± 1.6
	♀	38.3 ± 0.6	39.9 ± 1.9	40.7 ± 1.2	45.3 ± 1.2**
Histopathology					
nose atrophy of olfactory epithelial cells	♂	0/5	0/5	1/5 very slight	2/5 very slight + 3/5 slight, plane of section III
	♀	0/5	0/5	1/5 very slight	2/5 slight + 3/5 moderate, planes of section III + IV

Table 1 (continued)

Study parameters	Exposure concentration			
Study 2: 10 ♂ each	**0 ml/m³**	**150 ml/m³**	**500 ml/m³**	**1500 ml/m³**
initial body weight [g]; AV ± SD	124 ± 1.9	124 ± 1.9	124 ± 1.9	124 ± 1.9
body weight at end of study [g]; AV ± SD	238 ± 9.0	231 ± 8.0	237 ± 6.0	245 ± 5.2
increase in body weight [g]	113	107	114	122
prothrombin time [sec]; AV ± SD	37.8 ± 0.4	37.9 ± 0.7	38.6 ± 0.5	38.2 ± 0.5
white blood cells ($x10^{-9}$/l); AV ± SD	13.1 ± 0.5	13.4 ± 0.9	13.8 ± 0.8	14.8 ± 1.0
lymphocyte fraction	91.9%	87.2%	87.6%	90.6%
total protein [g/l]; AV ± SD	60.6 ± 0.5	60.3 ± 0.5	58.8 ± 0.6	59.5 ± 0.5

Significances reported in study: *: $p < 0.05$; **: $p < 0.01$, ANOVA and Dunnett's tests, two-sided; AV: average value; SD: standard deviation

Manifesto (MAK value/classification)

MAK value. In a 28-day inhalation study with exposure to methyl vinyl ether, the NOAEC for local effects on the olfactory epithelium in male and female rats and for systemic toxicity in female rats was 3500 ml/m³. At the very high concentration of 25 000 ml/m³, the only effects caused by the substance were a slight decrease in the number of olfactory epithelial cells in both sexes, a not significant reduction (to 95% of the control value) in body weights in female animals and a significant reduction in body weights in male animals. However, the absorption of methyl vinyl ether is already saturated to 75% at a concentration of 1500 ml/m³. In the male animals only, an increase in prothrombin time and a reduction in the lymphocyte count and protein content was observed at all concentrations; however, these effects were not dependent on the concentration. In a second study with 10 male animals per concentration group (twice as many male animals as in the preceding study), none of these effects were observed and no local or systemic effects were found up to the highest concentration tested of 1500 ml/m³. The findings from the second study call into question the effect on body weight gains in male rats described at 3500 ml/m³. The slight decrease in the number of olfactory epithelial cells at methyl vinyl ether concentrations of 25 000 ml/m³ are to be regarded as the beginnings of a local effect. There is a sufficiently large margin between the MAK value for methyl vinyl ether of 200 ml/m³ and the concentrations of ≥ 3500 ml/m³ at which these findings were observed – bearing in mind that saturation is reached at these concentrations – that exposure up to this level ensures protection even if the effect increases in magnitude over time, and the extrapolation of the findings from animal studies to humans and the additional increased body burden resulting from the increased respiratory volume of workers at the workplace are taken into consideration. For this reason, the MAK value for methyl vinyl ether of 200 ml/m³ has been retained.

Peak limitation. As the MAK value for methyl vinyl ether was derived from systemic effects, this substance remains classified in Peak Limitation Category II. There are no data available for the half-life of the substance. For this reason, the default excursion factor 2 has been retained.

Prenatal toxicity. There are no new data available. In a valid developmental toxicity study, delayed ossifications and slight variations were observed at a methyl vinyl ether concentration of 10 000 ml/m³. The NOAEC for developmental toxicity is 5000 ml/m³. At the same time, there was slight maternal toxicity. Even taking the increased respiratory volume (1:2) into account, the 13-fold difference between the NOAEC for developmental toxicity and the MAK value of 200 ml/m³ is sufficiently large that methyl vinyl ether remains classified in Pregnancy Risk Group C.

References

Andersen ME, Gargas ML, Jones RA, Jankins LJ (1980) Determination of the kinetic constants for metabolism of inhaled toxicants in vivo using gas uptake measurements. Toxicol Appl Pharmacol 54: 100–116

BG Chemie (1989 a) A sub-acute (28-day) vapour inhalation toxicity study of methyl-vinyl ether in rats. TNO-CIVO, No. V87.100, November 1989, BG Chemie, Heidelberg, unpublished report

BG Chemie (1989 b) A sub-acute (28-day) vapour inhalation toxicity study of methyl-vinyl ether in male rats. TNO-CIVO, No. V89.115, November 1989, BG Chemie, Heidelberg, unpublished report

BG Chemie (1989 c) Sub-acute (28-day) vapour inhalation toxicity study of methyl-vinyl ether in rats. TNO-CIVO, No. V89.158, summary of reports No. V87.100 and V89.115, November 1989, BG Chemie, Heidelberg, unpublished report

Buist HE, de Wit-Bos L, Bouwman T, Vaes WHJ (2012) Predicting blood:air partition coefficients using basic physicochemical properties. Regul Toxicol Pharmacol 62: 23–28

SRC (Syracuse Research Corporation) (2011) PhysProp database, http://esc.srcinc.com/fatepointer/search.asp

completed April 5, 2017