The MAK Collection for Occupational Health and Safety

N-Vinyl-2-pyrrolidone

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

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N-Vinyl-2-pyrrolidone / 1-Ethenylpyrrolidin-2-one

MAK Value Documentation

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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 N-vinyl-2-pyrrolidone [88-12-0].
N-Vinyl-2-pyrrolidone is a non-genotoxic carcinogen in liver, nose and larynx of rats. In 28-day inhalation studies it was shown that cell proliferation in liver and hyperplasia in the nasal epithelia of rats is increased at 0.5 ml/m³ with a NOAEC of 0.2 ml/m³. The former MAK value of 0.02 ml/m³ was derived from this concentration, the MAK value is now lowered to 0.01 ml/m³. This takes into account the increased respiratory volume at the workplace, because the blood:air partition coefficient of N-vinyl-2-pyrrolidone is > 5 (see List of MAK and BAT Values, Sections I b and I c). Since a systemic effect is critical, Peak Limitation Category II is retained. As the critical metabolite is not known, the default excursion factor of 2 for systemically acting compounds is confirmed.
For rats, the NOAEC for developmental toxicity after inhalation is 5 ml N-vinyl-2-pyrrolidone/m³, where reduced maternal body weight gain occurred. At 20 ml/m³ reduced foetal bodyweight and an increase of variations were observed. Taking into account the increased respiratory volume at the work place the NOAEC for developmental toxicity is 250 times higher than the MAK-value. Therefore, N-vinyl-2-pyrrolidone remains assigned to Pregnancy Risk Group C.

Keywords

N-vinyl-2-pyrrolidone; N-vinylpyrrolidone; N-vinylpyrrolid-2-one; 1-vinyl-2-pyrrolidone; N-vinylpyrrolidinone; 1-vinyl-2-pyrrolidinone; 1-ethenyl-2-pyrrolidinone; vinylbutyrolactam; (sub)chronic toxicity; developmental toxicity; peak limitation; prenatal toxicity; occupational exposure; maximum workplace concentration; MAK value; toxicity; hazardous substance

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N-Vinyl-2-pyrrolidone[1)]

[88-12-0]

Supplement 2018

MAK value (2017)	**0.01 ml/m³ (ppm) ≙ 0.046 mg/m³**
Peak limitation (2013)	**Category II, excursion factor 2**
Absorption through the skin (2004)	**H**
Sensitization	**–**
Carcinogenicity (2013)	**Category 4**
Prenatal toxicity (2013)	**Pregnancy Risk Group C**
Germ cell mutagenicity	**–**
BAT value	**–**
1 ml/m³ (ppm) ≙ 4.61 mg/m³	**1 mg/m³ ≙ 0.217 ml/m³ (ppm)**

Documentation for N-vinyl-2-pyrrolidone was published in 1991 (documentation "N-Vinyl-2-pyrrolidone" 1993), followed by supplements in 2004 (supplement "N-Vinyl-2-pyrrolidon" 2004) and 2014 (supplement "N-Vinyl-2-pyrrolidon" 2014).

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. However, this does not apply to gases or vapour with a blood:air partition coefficient < 5 (see List of MAK and BAT Values, Sections I b and I c). According to the formula of Buist et al. (2012), the blood:air partition coefficient of N-vinyl-2-pyrrolidone is > 5. This supplement evaluates whether the MAK value and the pregnancy risk group of N-vinyl-2-pyrrolidone need to be re-assessed as a result of the higher respiratory volume at the workplace.

1) The substance can occur simultaneously as vapour and aerosol.

Subacute, subchronic and chronic toxicity

Inhalation

There are no new data available.

In a 28-day inhalation study carried out according to OECD Test Guideline 412, groups of 8 male Wistar rats were exposed to N-vinyl-2-pyrrolidone concentrations of 0, 0.5, 5 or 10 ml/m³ to investigate cell proliferation in the liver, the target organ. Histopathological examination was performed on the nasal epithelium after haematoxylin and eosin (H&E) staining. As this study did not yield a NOAEC (no observed adverse effect concentration), additional animals were exposed to concentrations of 0, 0.2 or 0.5 ml/m³. At 0.5 ml/m³ and above, concentration-dependent cell proliferation in the liver and degeneration, hyperplasia and squamous metaplasia in the nasal epithelium were observed; the NOAEC in both organs was 0.2 ml/m³. There were no substance-induced clinical symptoms, nor were mortality, changes in relative organ weights, macroscopic changes or histopathological findings beyond those of the liver and nose observed. After exposure for 7 days, the NOAEC for effects on the liver was 0.5 ml/m³ (BASF SE 2011).

Developmental toxicity

There are no new data available.

In a valid study of the developmental toxicity of N-vinyl-2-pyrrolidone in rats carried out according to OECD Test Guideline 414, exposure to concentrations of 0, 1, 5 or 20 ml/m³ led to reduced body weights and delayed ossification in the foetuses of the high concentration group. The NOAEC for developmental toxicity was 5 ml/m³. The corrected body weights of the dams were significantly reduced at this concentration; the NOAEC for maternal toxicity was 1 ml/m³ (BASF AG 2001; supplement "N-Vinyl-2-pyrrolidon" 2014).

Manifesto (MAK value/classification)

After inhalation exposure, a non-genotoxic carcinogenic effect was observed in the liver, nose and larynx of rats. The most sensitive end points were cell proliferation in the liver and degeneration and hyperplasia of the nasal epithelium.

MAK value. In a 28-day inhalation study in rats, cell proliferation in the liver and degeneration and hyperplasia of the nasal epithelium were observed at N-vinyl-2-pyrrolidone concentrations of 0.5 ml/m³ and above. The NOAEC in both organs was 0.2 ml/m³. Taking into consideration that the study period was only 28 days and that the NOAEC recorded for cell proliferation in the liver after 28-day exposure was lower than that recorded after 7-day exposure, a value of 0.02 ml/m³ is derived from this NOAEC after applying the procedure of the Commission (see List of MAK and BAT Values, Section I). To account for the increased body burden caused by the increased respiratory volume of the worker at the workplace, the MAK value for N-vinyl-2-pyrrolidone is reduced by half to 0.01 ml/m³.

Peak limitation. The MAK value was derived from a systemic effect and the critical metabolite has not been identified. For this reason, N-vinyl-2-pyrrolidone remains classified in Peak Limitation Category II with a default excursion factor of 2.

Prenatal toxicity. In a valid study of the developmental toxicity of N-vinyl-2-pyrrolidone in rats carried out according to OECD Test Guideline 414, the NOAEC for developmental toxicity was 5 ml/m^3. The corrected body weights of the dams were significantly reduced at this concentration; the NOAEC for maternal toxicity was 1 ml/m^3. The developmental toxicity occurs concurrently with maternal toxicity and the margin between the NOAEC of 5 ml/m^3 for developmental toxicity and the MAK value is sufficiently large; this means that the substance may be classified in Pregnancy Risk Group C. As there are no new data available and both the MAK value and the NOAEC for developmental toxicity have been reduced by half to account for the increased respiratory volume (1:2), the 250-fold margin between the NAEC (no adverse effect concentration) for developmental toxicity (2.5 ml/m^3) and the MAK value of 0.01 ml/m^3 remains valid. N-vinyl-2-pyrrolidone therefore continues to be classified in Pregnancy Risk Group C.

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