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Toxicological Summary for: N-Nitrosodimethylamine (NDMA)

CAS: **62-75-9**

Synonyms: Dimethylnitrosamine, Methanamine, N,N-dimethylnitrous amide (IUPAC)

Acute Non-Cancer Health Based Value ($nHBV_{Acute}$) = Not Derived (Insufficient Data)[#]

Short-term Non-Cancer Health Based Value ($nHBV_{Short\text{-}term}$) = Not Derived (Insufficient Data)[#]

Subchronic Non-Cancer Health Based Value ($nHBV_{Subchronic}$) = Not Derived (Insufficient Data)[#]

Chronic Non-Cancer Health Based Value ($nHBV_{Chronic}$) = Not Derived (Insufficient Data)[#]

[#]Statement on Non-Cancer Toxicity of NDMA:
MDH did not derive non-cancer water guidance for NDMA due to deficiencies in the available studies. Despite the study limitations, it is clear that NDMA is mutagenic and has the potential to cause health effects from less than lifetime exposures, particularly in early life, and can be transferred from the mother to her developing fetus (See footnote 2 on page 2.) Therefore, MDH suggests limiting shorter term exposures where possible to the level of the Cancer Health Based Value (cHBV) of 0.005 µg/L.

Cancer Health Based Value (cHBV) = 0.005 µg/L

$$\frac{\text{(Additional Lifetime Cancer Risk) x (Conversion Factor)}}{[(SF \times ADAF_{<2\ yr} \times IR_{<2yr} \times 2) + (SF \times ADAF_{2\text{-}<16\ yr} \times IR_{2\text{-}<16yr} \times 14) + (SF \times ADAF_{16+\ yr} \times IR_{16+yr} \times 54)] / 70}$$

$$= \frac{(1E\text{-}5) \times (1000\ \mu g/mg)}{[(21 \times 10^{*} \times 0.125\ L/kg\text{-}d^{**} \times 2) + (21 \times 3^{*} \times 0.045\ L/kg\text{-}d^{**} \times 14) + (21 \times 1^{*} \times 0.041\ L/kg\text{-}d^{**} \times 54)] / 70}$$

= 0.0049 rounded to **0.005 µg/L**

[*]ADAF (Age-dependent adjustment factor): MDH 2008, Section IV.E.2.
[**]Intake Rate: MDH 2008, Section IV.E.2. and US EPA 2011, Exposure Factors Handbook, Tables 3-1 and 3-81.

Cancer classification:	Likely to be carcinogenic to humans by a mutagenic mode of action for all routes of exposure (USEPA, 2016) Group 2A, probably carcinogenic to humans (IARC, 1987)
Slope factor (SF):	21 $(mg/kg\text{-}d)^{-1}$ (liver tumors in female Colworth-Wistar rats) (Peto, 1991a,b)
Source of cancer slope factor (SF):	USEPA, 2016 and Federal Register, 2014
Tumor site(s):	Liver

Volatile: **Yes (low)**

Summary of Guidance Value History:

MDH has not previously developed water guidance for NDMA.

Summary of toxicity testing for health effects identified in the Health Standards Statute (144.0751):

Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. MDH has considered the following information in developing health protective guidance.

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested for specific effect?	No	Yes	Yes	Yes	No
Effects observed?	-	Yes[1]	Yes[2]	Yes[3]	-

Comments on extent of testing or effects:

[1] One study examined immune effects following NDMA exposure where effects occurred at doses over 350,000 times higher than the cancer-based dose, corresponding to a 1:100,000 risk level. In this immune study a decrease in immune cell response was noted.

[2] A few studies of limited design and reporting have examined developmental toxicity. In a single dose drinking water study, an increase in neonatal deaths and stillbirths was noted at the dose tested, which was nearly 7,000 times higher than the cancer-based dose, corresponding to a 1:100,000 risk level. Due to data limitations and frank effects occurring at the 7,000-fold higher dose level, the likelihood of additional subtle adverse effects from the transfer of NDMA to the fetus at lower dose levels is an outstanding concern. Therefore, the 7,000-fold difference between the dose associated with frank developmental effects and cancer guidance would likely be smaller if sufficiently-designed developmental studies were available.

[3] A small number of studies limited in design and reporting have observed reproductive effects. At a dose nearly 7,000 times higher than the cancer-based dose, corresponding to a 1:100,000 risk level, alterations in the sex ratio of offspring in rats were noted. High dose gavage studies, with NDMA exposures over 250,000 times higher than the cancer-based dose resulted in decreased fetal and maternal weight, embryo loss, and maternal deaths. These deleterious effects occurred in studies conducted at a very limited number of high dose levels. The likelihood of more subtle adverse effects at lower dose levels is a significant outstanding concern. Male reproductive toxicity was also observed in an intraperitoneal injection study at high doses (this route of exposure is not directly comparable to oral exposures).

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