

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

October 26, 2015

TO: File for N-Nitroso-N-methylurea (CAS # 684-93-5)
FROM: Mike Depa, AQD Toxics Unit
SUBJECT: Screening level Update for N-Nitroso-N-methylurea

The inhalation unit risk (IUR) for N-Nitroso-N-methylurea is changing at this time. The former IUR for N-Nitroso-N-methylurea and the resulting Initial Risk Screening Level (IRSL) and Secondary Risk Screening Level (SRSL) were derived in a May 17, 1993 memorandum (see attached memo from Gary Butterfield).

The U.S. Environmental Protection Agency (EPA, 2005) provides guidance for the appropriate adjustment of the IUR for carcinogens with a mutagenic mode of action. This approach was evaluated and endorsed by the MDEQ Toxics Steering Group (TSG, 2012). According to EPA (2005), for chemicals that have been determined to have a mutagenic mode of action (MOA) for carcinogenesis, chemical-specific information should be used to develop cancer slope factors that address any potential for differential potency in early life stages, if appropriate data are available. If appropriate chemical-specific data are not available, then the default age-dependent adjustment factors (ADAFs) should be applied to the IUR (EPA, 2005). To calculate life-time risk for a population with average life expectancy of 70 years, the IUR that is protective of childhood exposure is calculated from the sum the risk associated with each of these three time periods:

- Risk for birth through < 2 yr = (IUR) x 10 (ADAF_{<2yr}) x (2yr/70yr)
- Risk for ages 2 through < 16 = (IUR) x 3 (ADAF_{2 - <16yr}) x (13yr/70yr)
- Risk for ages 16 until 70 = (IUR) x 1 (ADAF_{16 - 70yr}) x (55yr/70yr)

It has been determined by EPA that N-Nitroso-N-methylurea has a mutagenic MOA (EPA, 2015). Since appropriate chemical-specific data are not available for N-Nitroso-N-methylurea, the default ADAF (EPA, 2005) for life-time exposure was applied to the adult-based IUR using the procedure below.

Summing the above age specific ADAFs, the overall life-time ADAF is a factor of 1.6-fold. The ADAF adjustment for constant life-time exposure under standard exposures is applied to the IUR, as follows:

$$\begin{aligned} \text{IUR}_{\text{life-time}} &= \text{IUR}_{\text{adult}} \times 1.6 \\ \text{IUR}_{\text{life-time}} &= 0.6 \text{ per } \mu\text{g}/\text{m}^3 \times 1.6 \\ \text{IUR}_{\text{life-time}} &= 1.0 \text{ per } \mu\text{g}/\text{m}^3 \end{aligned}$$

Pursuant to Rule 231(1), the IRSL and SRSL are then calculated as follows:

$$\begin{aligned} \text{IRSL} &= \frac{1\text{E-6 risk}}{1.0 (\mu\text{g}/\text{m}^3)^{-1}} = 1 \text{ E-6 } \mu\text{g}/\text{m}^3 \text{ (annual averaging time)} \\ \text{SRSL} &= \frac{1\text{E-5 risk}}{1.0 (\mu\text{g}/\text{m}^3)^{-1}} = 1 \text{ E-5 } \mu\text{g}/\text{m}^3 \text{ (annual averaging time)} \end{aligned}$$

References

EPA, 2005. Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. Risk Assessment Forum U.S. Environmental Protection Agency Washington, DC. EPA/630/R-03/003F: http://www3.epa.gov/ttn/atw/childrens_supplement_final.pdf

EPA, 2015. Regional Screening Table. Superfund Program. U.S. Environmental Protection Agency. June 2015 Update. Accessed 10-26-15. <http://www2.epa.gov/risk/regional-screening-table>

TSG, 2012. Evaluation of Age-Dependent Adjustment Factors (ADAFs) Application Toxics Steering Group, Children's Environmental Health Subcommittee February 9, 2012 (Mistakenly dated 2/9/2011 on title page).

MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

May 17, 1993

To: N-Nitroso-N-methylurea File (CAS # 684-93-5)
From: Gary Butterfield
SUBJECT: IRSL/SRSL for N-Nitroso-N-methylurea

N-Nitroso-N-methylurea or NMU is also known as N-methyl-N-nitrosourea. EPA's IRIS database lists this material as being under review. There are numerous studies providing evidence of NMU's carcinogenicity. However, there are limitations (short dosing period, non-natural route of administration, etc.) which preclude their use for calculating quantitative risk estimates.

EPA'S Feb 21, 1991 Boiler and Industrial Furnace regulations for burning of hazardous waste lists a unit risk of $8.6E-2 (\mu\text{g}/\text{m}^3)^{-1}$ for NMU. However there was no data given or able to be located that supports this unit risk value.

As a result of a personal conversation with Dennis Pagano of EPA'S OAQPS in RTP it was possible to obtain a 1988 document from EPA'S OHEA carcinogen assessment group. This document identifies an oral slope factor of $2100 (\text{mg}/\text{kg})^{-1}$. This slope factor can be converted to an inhalation slope factor of $0.6 (\mu\text{g}/\text{m}^3)^{-1}$, which results in an IRSL of $1.7 E-6 \mu\text{g}/\text{m}^3$.

Due to no long and detailed evaluation having been conducted by AQD toxicologist on NMU, this IRSL will appear on the interim list.

References:

EPA. 1991. BIF Hazardous waste burning. 56 FR 7134-7239. Thursday Feb 21, 1991. See the table on page 7233.

EPA. 1988. Evaluation of the potential carcinogenicity of N-Nitroso-N-methylurea, in support of the reportable quantity adjustments pursuant to CERCLA Section 102. OHEA-C-073-152 final. June 1988.

Pagano, Dennis. Feb 23, 1993. EPA'S OAQPS Pollutant Assessment Branch, personal communication (919) 541-0502.