**MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY**

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**INTEROFFICE COMMUNICATION**

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June 24, 2010

TO: File for 3-Methoxy-3-Methyl-1-Butanol (CAS# 56539-66-3)

FROM: Michael Depa, Toxics Unit, Air Quality Division

SUBJECT: Screening Level Determination for 3-Methoxy-3-Methyl-1-Butanol

The initial threshold screening level (ITSL) for 3-methoxy-3-methyl-1-butanol (MMB) is 13 µg/m³ based on an annual averaging time.

The following references or databases were searched to identify data to determine the screening level: U.S. EPA Integrated Risk Information System (IRIS), Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), National Institute for Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online (1967- May 2003), National Library of Medicine (NLM), Health Effects Assessment Summary Tables (HEAST), and National Toxicology Program (NTP) Status Report. The EPA has not established a reference dose (RfD) or a reference concentration (RfC) for 3-methoxy-3-methyl-1-butanol. There are no occupational exposure limits (e.g., ACGIH TLV or NIOSH REL). The molecular formula is $C_6H_{14}O_2$. The molecular weight of 3-methoxy-3-methyl-1-butanol is 118.2g.

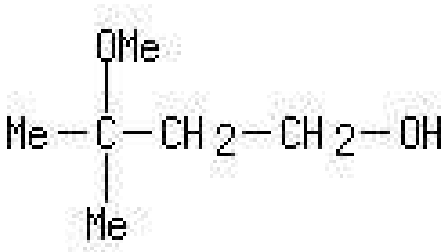


**Figure 1. Molecular Structure of 3-Methoxy-3-methyl-1-butanol (MMB)**

**Toxicological Reports**

CBC America Corporation sent MDEQ-AQD a toxicological summary from Kuraray Co (1991).

In a mutagenicity study, no substantial increases in revertant colony number for any of the 6 tester strains were observed following treatment with MMB at any dose level, either in the presence or the absence of metabolic activation (Kuraray Co., 1991).

In an acute oral toxicity study, groups of 5 male and female rats were dosed with MMB at levels of 2.0, 3.2, 4.0, and 5.0 g/kg and observed for 15 days (Kuraray Co., 1991). Neurological related observations included: lethargy and pallor of extremities, abnormal body carriage (hunched), abnormal gait (waddling), ataxia and decreased respiration rate and ptosis. A slightly pale cortex of the kidney was observed in 3 males and 3 female in the 5.0 g/kg group and one female in the 4.0 g/kg dose group. The LD50 (95% confidence limits) were reported:

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| Males and Females: | 4.4 (3.9-5.2) g/kg |
| Males: | 4.5 (3.9-5.6) g/kg |
| Females: | 4.3 (3.6-5.3) g/kg |

In an oral developmental toxicity study, a total of 48 presumed pregnant rates were tested (Kuraray Co., 1991). MMB was administered (gavage or feed route not specified) on Days 6-15 of presumed gestation at dosages of 0, 125, 250, 500, 1000 or 2000 mg/kg/day. Eight (8) rats were randomly assigned to each dosage level. Clinical observations showed one high dosage rat was ataxic on day 9 of gestation. No other clinical observations or necropsy observation were attributed to MMB. One high dose rat had gasping on Days 17-20 of gestation and rales on Day 19 of gestation. Necropsy of this rat showed evidence of reduced feed consumption, little fecal matter in the intestines, gas-filled stomach and intestines. Other observations made mentioned excess salivation, chromodacryorrea, localized alopecia, and a swollen, purple limb. One non-pregnant dosage-group rat had a fluid-filled cyst on the serosal surface of the cervix; however, the authors did not attribute this finding to MMB dosing. Body weight gains were reduced for the dosage period in groups given 500-2000 mg/kg/day. The 1000 mg/kg group had weight loss on Days 6-7 of gestation, while the 2000 mg/kg group showed weight loss on Days 6-9 of gestation. The 2000 mg/kg dose group also showed reduced weight gain during the post-dosage period (Days 16-20). Average body weights and body weight gains of the dams were unaffected at dose levels as high as 250 mg/kg/day. The absolute and relative maternal feed consumption values decreased for the 2000 mg/kg/day group during both the dosage and post dosage periods. The average fetal body weights were reduced in the 1000 and 2000 mg/kg/day dosage groups. However, no other caesarian-sectioning or litter parameters (such as averages for corpora lutea, implantations, litter sizes, resorptions, fetal sex ratios and percent resorbed conceptuses) were affected. The authors stated that dosages of MMB up to 500 mg/kg/day affected neither the dams nor their litters. Two incidences of gross external fetal alterations were observed. One 250 mg/kg/day fetus had depressed eye bulges and agnathia. One 500 mg/kg/day fetus had a misshapen head on which there was a hematoma. The authors stated that neither of these alterations was attributed to MMB. No other fetal alterations were observed.

In an inhalation study, groups of 10 male rats were dosed at 0, 100, 300 or 500 ppm MMB (0, 483, 1450, 2417 mg/m$^3$) for 4 hours per day, 5 days per week for 4 weeks (Kuraray Co., 1991). Organ weights, histomorphological examinations of organs, blood and urine analysis was performed. No animals died prior to sacrifice. No changes in clinical observations were observed. There were no differences in weight growth or food and water consumption. The authors stated that post-mortem examination revealed a slight congestion in the lungs of most animals. A slight bleeding region of the lung parenchyma was noted in one animal each of the 500 ppm group and the reference group and was not attributed to MMB exposure. No specific changes were observed in the spleen, adrenal gland, heart, testicles, brain or vertebra. A significant

increase in kidney weight among the tested animals was observed, but no wide differences were noted between the control and test groups in the functional inspection of the kidney. A microfibrinous region on the cortical under-membrane was noted in two animals each of the 500 ppm and 300 ppm groups, respectively, in three animals of the 100 ppm dosage group, and in one animal of the reference group. One slight lymphocyte infiltration region in the stroma of the cortex was noted in one animal in each of the 500 ppm and 300 ppm groups, and slight lymphocyte infiltration in the renal pelvis membrane was observed in one animal of the reference group. No functional disease of the liver was observed other than increased glutamic-oxaloacetic transaminase (GOT). Some regions of necrotized cells were observed in one animal in each of the 300 ppm and 500 ppm dosage groups, as well as in two animals at the 100 ppm dose level. These regions were observed in only one or two areas of the membrane, however, so no correlation to MMB was made. The authors conclude that no significant changes were caused by exposure to MMB. The GOT and weight of kidney creased by comparison with the reference dose. The authors stated that the liver and kidney were slightly affected by MMB.

**Discussion**

The most appropriate study for assessing inhalation toxicity was the 4 week inhalation study in rats. The lowest dose level of 483 mg/m$^3$ (100 ppm) was determined to be an adverse effect level based on increased kidney weight, with microfibrinous regions on the cortical under-membrane. The designation of the 483 mg/m$^3$ dose level as a lowest-observed-adverse-effect-level (LOAEL) was further supported by the significant increase in GOT levels at this level, however, the mid-dose rats did not have increased GOT. Kidney effects were also observed in the 5.0 g/kg dose level of the LD50 study.

The screening level was calculated based on a modified Rule 232(1)(d); the 7-day inhalation LOAEL equation, where the uncertainty factor of 35 was reduced to 20 because the 4 week study was longer than the equation designed for a 7-day study. The LOAEL-to-NOAEL uncertainty factor was also reduced from 10 to 3 for mild effects.

ITSL = LOAEL/(20x100x3) x (hrs of exposure per day)/(24 hrs per day)

ITSL = 0.0013 mg/m$^3$

ITSL = 13 µg/m$^3$

Based on Rule 232(2)(c), the averaging time is “annual.” Therefore, the ITSL for 3-methoxy-3-methyl-1-butanol is 13 µg/m$^3$ based on annual averaging time.

**References**

Kuraray Co. (1991). Letter to Ms. Doris Sweet of National Institute of Occupational Safety and Health (NIOSH) dated December 6, 1991 from Koichi Yoshida of the Kararay Co., Tokyo, Japan. Obtained via fax from Ms. Akki Sampson of CBC (America) Corp., Chemical & Pharmaceutical Division, 55 Mall Dr., Commack, NY 11726.

MD:LH