MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

February 3, 2017

TO: Dimethylacetamide File (CAS No. 127-19-5)

FROM: Mike Depa, Air Quality Division, Toxics Unit

SUBJECT: Derivation of Initial Threshold Screening Level

The initial threshold screening level (ITSL) for dimethylacetamide (DMAC) is 100 µg/m³, with annual averaging time.

Previously, the averaging time (AT) assigned to the DMAC ITSL was 24 hours, pursuant to Rule 232(2)(b) of the Air Pollution Control Rules promulgated at that time (July 7, 2011; see attached memo). The recently promulgated (December 22, 2016) Air Pollution Control Rule 232(2)(b) states that ITSLs based on Rule 232(1)(a) are assigned an annual averaging time. An updated literature review was not performed at this time.

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

July 7, 2011

TO: File for Dimethylacetamide (CAS No. 127-19-5)

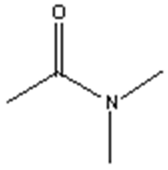
FROM: Michael Depa, Toxics Unit, Air Quality Division

SUBJECT: Screening Level Determination

The initial threshold screening level (ITSL) for dimethylacetamide (DMAC) is 100 µg/m³ (24-hour averaging time).

The following references or databases were searched to identify data to determine the screening level: Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS), the Registry of Toxic Effects of Chemical Substances (RTECS), the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), National Institute of 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- July 2011), 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 concentration (RfC) or reference dose (RfD) for dimethylacetamide. The ACGIH established a TLV for dimethylacetamide at 36 mg/m³ (10 ppm). NIOSH established a recommended exposure level (REL) of 35 mg/m³ (10 ppm). The molecular weight is 87.12 g, and the molecular formula is C_4H_9NO. The melting point is -20°C and the boiling point is 166°C. The vapor pressure is 9 mmHg @ 60 °C and 1.5 mmHg at 20°C. Dimethylacetamide is miscible in water at ≥100 mg/ml @ 22°C. This compound is a colorless liquid with a faint ammonia-like odor. The molecular structure is shown in Figure 1.

Figure 1. Molecular Structure of Dimethylacetamide (DMAC)



Occupational Exposure Limits (OELs)

The ACGIH and NIOSH developed a TLV for DMAC at 10 parts per million (ppm). The ACGIH documented several human studies. The ACGIH stated:

> Jaundice has been observed to result in workers exposed repeatedly at from 20 to 25 ppm DMA, but appreciable skin penetration undoubtedly contributed to this effect.[1] Workers exposed to DMA for 2-10 years showed abnormal liver function; exposure concentrations were not reported in the study.[2] DMA concentrations between 0 and 2 ppm, with occasional excursions between 11 ppm and 34 ppm, in a

[1] Johnson, M.N.: Letter from Medical Director of Chemstrand Corp. to the TLV Committee (March 1961).
[2] Corsi, G.C.: Dimethylacetamide-Induced Occupational Diseases with Particular Attention to Hepatic Function. Med. Lav. 62:28-30 (1971).

polymer manufacturing operation caused dizziness, lethargy, and weakness.[3] Concentrations between 0 and 3 ppm in metal finishing caused the same symptoms.[3]

Review Articles

In a review article (CRC, 1986), the LD50 acute oral toxicity of dimethylacetamide was reported as 2.6 to 4.9 g/kg in the mouse, and 2.25 to 10 g/kg in the rat. Reproductive, developmental or teratologic toxicity (oral) was observed in the hamster ("anitfertility"), rat ("embryotoxic, teratogenic at maternally toxic dose"). In the rat there was no "embryotoxc or teratogenic" effects observed via inhalation (dose not given). A study was reviewed that found no carcinogenic effects at doses up to 30 mg/kg. However, this study was performed for less than 1 year, not the standard 2 years.

Metabolism, Excretion and Pharmacokinetics

Male volunteers were exposed via inhalation (10 ppm) and skin (375 mg) for 6 hours (Maxfield et al., 1975). Urine was collected and analyzed for the presence of monomethylacetamide (MMAC). MMAC was measured as early as 2 hours after exposure. Trace amounts, up to 2 ppm MMAC, were found in all but one of the 16 samples collected three and five days after the exposure. The authors stated that 70% of the excreted metabolite could be attributed to absorption through the lungs and 30% to skin absorption.

Groups of male CD rats and CD-1 mice were exposed to either single or multiple exposures to 50, 150, 300 or 500 ppm DMAC (Hundley et al., 1994). In the animals exposed to a single 6-hour period, blood samples were taken 1, 2, 4, 6, 8, 12 and 24 hours post-exposure. Four mice were sacrificed at each time interval and blood samples were taken by cardiac puncture. Serial blood samples from 4 rats in each exposure group were collected from the tail-vein. Urine samples were collected from rodents used for the 24-hour blood samples and were collected at 12 and 24 hours. In addition, 1- and 3-hour exposures were conducted in order to estimate the increase in DMAC plasma levels at intermediate time points during a 6 hours exposure. Blood samples were taken approximately 0.5 hours after termination of exposure. For multiple exposures, rats and mice were exposed 6 hr/day, 5 days/week for two weeks. Each group consisted of 8 rats and 32 mice. Plasma profiles indicated mice metabolized DMAC rapidly with plasma half-lives from 0.3 to 0.5 hours. MDMAC plasma half-lives in rats ranged from 0.6 to 1.5 hours. The area under the curve values for DMAC in rats increased approximately 5-fold and 3-fold as exposure concentrations in creased from 150 to 300 ppm and 300 to 500 ppm exposures to rats. Regardless of exposure level, repeated DMAC exposures to both rats and mice resulted in plasma profiles of DMAC similar to those from a single exposure. The authors concluded that the dose-dependent nature of the DMAC AUC data and the effects of repeated 300 and 500 ppm DMAC exposures supported a toxicity-driven upper limit of 350 ppm for a chronic inhalation study.

Acute Studies

The 1-hr LC50 of DMAC was reported as 2475 ppm (8821 mg/m3) (Kennedy, et al, 1986).

Reproductive and Developmental Studies

In an inhalation developmental study, groups of 15 pregnant Himalayan rabbits were exposed to DMAC vapors at concentration of 0, 200, 700 or 2000 mg/m³ for 6 hrs/day from day 7 to 19 postimplantation (Klimisch and Hellwig, 2000). In a satellite study, groups of 5 rabbits were exposed to 0 or 2000 mg/m³ for 6 hrs/day from day 7 to 19 postimplantation. All animals were observed until day 29 postimplantation. No signs of maternal toxicity were seen in the does of the main groups (body weight and gross pathology) or in the does of the satellite groups (body weight, blood chemistry, histopathological finings of the liver). Fetotoxic effects were caused at a concentration of 700 mg/m³ (e.g., increased skeletal variation) and 2000 mg/m³ (significantly decreased fetal and placental weights, increase in soft tissue and skeletal variations). For maternal effects the no-

[3] Wang, J.C.: Studies on the Maximum Allowable Concentration of N,N-Dimethylacetamide. Chung-hau Yu Fang I Hsuch Tsa Chih 13:29 (abstract)(1979).

observable-adverse-effect-level (NOAEL) was 2000 mg/m^3. For developmental effects the NOAEL was 200 mg/m^3.

Groups of 25 CD rats were exposed to 0, 30, 100 or 300 ppm DMAC from days 6 to 15 of gestation 6 hrs/day (Solomon et al., 1991). At 282 ppm, both maternal weight gain during the exposure period and fetal weight were significantly decreased and accompanied by a significant dose-response trend. Fetal resorptions were not increased in any of the groups exposed to DMAC. Fetal incidences of external, visceral, or skeletal variations and malformations were similar between the test and control groups. Therefore, both fetal and maternal toxicity were noted at the 282 ppm and the no-observed-adverse-effect-level under these conditions was 100 ppm for both the dam and the conceptus.

In a reproductive study, groups of 10 male and 20 female CD rats were exposed to 0, 32, 100, or 282 ppm DMAC for 6 hrs/day, 5 days/week for 10 weeks prebreeding, the 7 days/week for 7 to 8 weeks (through breeding, gestation, and lactation)(Ferenz and Kennedy, 1986). The exposure period was interrupted for female rats between gestation Day 21 and postpartum Day 4. No compound-related effects on body weigh, survival, or clinical signs were detected in parental rats. Liver weight to body weight ratios were increased in groups where both males and females were exposed to 300 ppm but not in groups where only male or only females were exposed to 300 ppm No significant differences were observed between control and test rats with respect to mating performance, fertility, length of gestation, progeny numbers, structure, and viability. At 21 days postpartum, pups derived from matings involving exposure of both sexes to 300 ppm or exposure of parental females to 300 ppm had lower body weights than did the controls. Gross pathological examination of representative pups and evaluation of liver and gonad weight data did not reveal any DMAC-related changes. The authors concluded that reproduction in rats was not altered by repeated inhalation exposure to up to 300 ppm DMAC.

In a male fertility study, groups of 12 male Sprague-Dawley rats were exposed to 0, 40, 120 or 400 ppm DMAC for 6 hrs/day, 5 days/week (Wang et al., 1989). Treatment-related effects of increased liver weights and liver/body weight ratios were observed in the 120 and 400 ppm dose groups ($p<0.05$ and $p<0.01$, respectively). Clinical chemistry analysis indicated no significant differences between any of the treatment groups and the control group. There were no treatment-related effects on the histopathology of the liver, kidneys or testes. There were no treatment related effects on the number of copulations, live fetuses, fetus weights, resorptions or corpora lutea.

Developmental toxicity of N,N-dimethylacetamide (DMAC) was examined by exposing pregnant rats by inhalation to DMAC vapor at 0, 100, 300, 450 or 600 ppm for 6 h/d during Gestation Days 6 through 19 (Okuda et al., 2006). Fetal body weight and the number of male live fetuses were significantly decreased, along with a tendency of the number of intrauterine deaths to increase. The number of fetuses with visceral and skeletal malformations was significantly increased in the 450 and 600 ppm groups, while the number of fetuses with anasarca as an external malformation was increased at 600 ppm. Observed cardiovascular malformations included ventricular septum defect, persistent truncus arteriosus, malpositioned subclavian branch and retroesophageal subclavian artery. Persistent truncus arteriosus was accompanied by ventricular septal defect (VSD). Incidences of the persistent truncus arteriosus, which was classified as a serious congenital heart disease affecting postnatal survival, were increased at 450 and 600 ppm. Increased liver weights and hepatocellular swelling occurred in the dams exposed to 300 ppm and above, whereas neither hepatocellular necrosis nor increased serum activity of liver transaminases was observed in any of the exposed groups. Maternal body weights were decreased at 450 and 600 ppm. The most sensitive signs of developmental toxicity appeared at the exposure level of 300 ppm which was also the level of slight maternal toxicity. The No-Observed-Adverse-Effect-Level (NOAEL) was determined as 100 ppm for the endpoints of fetal and maternal toxicities.

Subacute and Subchronic Studies

Groups of 10 male Crl:CD-1 BR mice (35 days old) were exposed 6 hours per day, 5 days per week for 2 weeks to target concentrations of 0, 30, 100, 310, 490 or 700 ppm DMAC (Valentine et al.,

1997). At the end of the study, 5 animals from each group were killed, the remaining animals from each group were observed for a 14-day non-exposure recovery period. In a supplemental study, groups of 9 to 13 older male Crl: CD-BR mice (61 days old) were exposed to 0, 50, 150, 300 or 500 ppm DMAC for 6 hours per day, 5 days per week for 2 weeks. Additionally, groups 9 to 13 male Crl: CD-BR rats (47 days old) were exposed to 0, 50, 150, 300 or 500 ppm DMAC for 6 hours per day, 5 days per week for 2 weeks.

Results from the 35 day old mice: Animals were examined for gross lesions at necropsy. The organs were weighed and analyzed histopathologically. Two of 10 mice from the 490 ppm group were killed in extremis within 6 days of study initiation, while 8 of 10 mice exposed to 700 ppm were either killed in extremis or found dead during the exposure period. No compound related clinical signs of toxicity were noted in groups exposed to 30, 100 or 310 ppm DMAC. At concentrations of 490 ppm DMAC or more, however, clinical signs including exophthalmos, labored or irregular respiration, weakness or lethargy, incapacitation, and tremors were typically seen either prior to exposure or upon unloading mice immediately after exposure. While some clinical signs were suggestive of central nervous system involvement (e.g., tremors, incapacitation, or lethargy), these signs were noted only in moribund mice. The body weights of the mice exposed to 700 ppm were statistically lower than that of control mice ($p<0.05$). Mice in the 30, 100 or 310 ppm groups did not have any biologically significant hematologic finding following either the exposure or the recovery periods. There were significant effects in red blood cell parameter and platelet counts found in mice from the 490 and 700 ppm groups ($p<0.05$). Significant ($p<0.05$) organ weight differences were present in testes, liver, and lungs of mice exposed to 490 ppm; an insufficient number of mice was available for statistical evaluation of organ weight data of mice from the 700 ppm group. After a 14-day recovery period, mean relative and absolute testes weights of mice from the 490 ppm group were significantly lower than control. By the end of the recovery period, both mean relative and absolute liver weights were significantly higher than controls. No treatment-related microscopic changes were present in mice exposed to either 30 or 100 ppm DMAC. Microscopic lesions were found in the testes of mice from the 310, 490 and 700 ppm groups and in the liver, bone marrow, lymphoid organs, and adrenal glands of mice exposed to 490 or 700 ppm DMAC. Lymphoid atrophy and/or necrosis was present in one or more lymphoid organs (i.e., mesenteric lymph node, spleen, or thymus) in 5 or 6 mice from the 490 ppm group and in 9 of 9 mice from the 700 ppm group.

Supplemental Study: All rats and mice exposed to either 0, 52, 150, 300 or 480 ppm DMAC survived the 10 exposures and showed no signs of clinical abnormalities. Body weights of all DMAC-exposed mouse groups compared favorable to those of the controls, while rats exposed to 480 ppm had depressed weight gain. Gross pathologic examination revealed no changes that could be related to DMAC exposure. Testes weights of mice exposed to 480 ppm DMAC were lower than those of the corresponding controls; no differences were seen in rat testes weights. No testicular changes were seen microscopically in rats or in mice exposed to 300 ppm or less. At 480 ppm, minimal to mil bilateral degeneration and atrophy of seminiferous tubules were seen in 3 or 9 mice. Testicular sperm counts were unchanged in all test groups compared to controls in both rodent species. The authors stated that:

> Despite the facts that no significant body or organ weight changes were noted at 310 ppm and that testicular atrophy may occur spontaneously in mice, based on the qualitatively similar testicular pathology found in mice exposed at this and higher concentrations, 310 ppm DMAC was considered to be a minimal effect level for testicular injury.

The authors concluded that:

> Under the condition of these studies that no-observable-adverse-effect-level for repeated exposure to DMAC in male mice was 100 ppm in pubescent mice and 300 ppm in more mature mice. At the non-lethal concentration of 300 ppm, the primary organ system affects by DMAC in pubescent mice was the testes, while at lethal exposure concentrations, pathologic effects also occurred in the bone marrow, the lymphoid organs, the adrenal cortex, and the liver. Very young mice appeared to be more sensitive to the testicular effects of DMAC than either rats or older mice.

In a two-week inhalation study, groups of 15 male CD rats were exposed to 0, 10, 30, 100 or 300 ppm DMAC for 3, 6 or 12 hrs/day for 5 days/week (Kinney et al., 1993). One-half of the rats in each group was allowed a 14-day post-exposure period to evaluate the reversibility of the DMAC-induced changes. No clinical signs of toxicity or DMAC related gross changes at necropsy were seen in any of the rats. Body weights were significantly decrease ($p<0.05$) in the 300 ppm dose group at the 6 and 12 hrs/day exposure durations, but returned back to normal at day 7 and 14 of recovery. Increases in serum cholesterol were seen in rats exposed to either 100 or 300 ppm DMAC whether the exposures were 3, 6 or 12 hours per day ($p<0.05$) and in the 30 ppm dose group at 13 hours per day ($p<0.05$). Serum total protein concentrations were increased in rats exposed for 12 hours per day to either 30, 100 or 300 ppm DMAC. None of these changes were seen in the rats allowed to recover for 14 days. Absolute and relative liver and testes weights were not significantly different from controls. Microscopically, DMAC produced changes in the liver at 300 ppm at 12 hours per day. These changes persisted after recovery. No treatment related changes were seen in the testes and nasal passages.

Chronic Studies

In a six-month inhalation study, groups of 2 dogs and 4 rats (strain not reported) were exposed to 0, 40.0, 64.4, 103, and 195 ppm DMAC for 6 hrs/day, 5 days/week (Horn, 1961). At the highest concentration rats presented an unkempt appearance with red-tinged discharge around the eyes. The experimental rats did not gain as much weight as the control animals. Survival among the experimental rats in all groups was as good as or better than among the controls. No changes in hemoglobin, sedimentation rates, hematocrit, or total and differential white blood cell counts were seen in any dog. Likewise, no differences were observed in the result of the urine analysis performed on the dogs during the study. Altered biochemistries consisting of BSP retention and elevated alkaline phosphatase were observed at the higher levels, but not at the two lower levels, 40 and 64 ppm. At all concentrations, no changes were noted in blood urea nitrogen (BUN) determinations or thymol turbidity tests. DMAC in the blood of the dogs exposed to the two lower concentrations were quite low, but in dogs exposed to the higher concentrations there were substantial. However DMA blood levels returned to baseline values overnight. The livers of all exposed dogs showed degeneration of the liver cord cells which was apparently periportal fatty metamorphosis; the 40 and 64 ppm dose level showed this effect but to a lesser degree. Microscopic examination of liver sections of rats exposed to 195 ppm showed varying degrees of cytoplasmic disturbance, cholangitis, periangitis, and small discrete areas of focal necrosis of the parenchymal cells. At the 103 ppm dose level, 3 of 5 rats examined showed significant liver cell degeneration, while the remaining two showed only mild changes. At the 64 and 40 ppm dose level, livers were not significantly different from control rats. Changes in the lungs of all rats were difficult to evaluate because of pneumonia. Dogs appear to be more sensitive than rats to the hepatotoxic effects of DMAC.

In another chronic exposure study, groups of 87 male and female CD rats and groups of 78 male and female CD mice were exposed by inhalation to 0, 25, 100, or 350 parts per million (ppm) DMAC 6 hrs/day, 5 days/week for 18 months (mice) or 2 years (rats) (Malley et al., 1995). An interim euthanization for rats occurred at 12 months and hepatic cell proliferation in rats and mice was examined at 2 weeks and 3 and 12 months. No compound-related effects on survival were observed. Rats exposed to 350 ppm had lower body weight and/or body weight gain. There were no compound related effects on body weight or weight gain in mice at any concentration. There were no compound related adverse effects on the incidence of clinical signs of toxicity in rats or mice. No hematologic changes were observed in either species. Serum sorbitol dehydrogenase activity was increase in rats exposed to 350 ppm. Serum cholesterol and glucose concentrations were significantly higher in 100 and 350 ppm female rats. Compound-related morphological changes were observed in the liver. In rats, exposure to 100 or 350 ppm produced increased absolute and/or relative liver weighs, hepatic focal cystic degeneration, hepatic peliosis, biliary hyperplasia (350 ppm only), and lipofuscin/hemosiderin accumulation in Kupffer cells. In mice, exposure to 100 or 350 ppm produced increased absolute and relative liver weights (350 ppm females only), accumulation of lipofuscin/hemosiderin accumulation in Kupffer cells, and centrilobular single cell necrosis. Male rat exposure to 350 ppm also had significantly higher absolute and relative kidney weights which

correlated with the gross and microscopic changes resulting from a compound-related increase in severity of chronic progressive nephropathy. Female mice exposed to 350 ppm had an increased incidence of bilateral, diffuse retinal atrophy. No increase in hepatic cell proliferation was seen in mice or rats at any exposure concentration. The authors stated that DMAC was not oncogenic under these experimental conditions in either the rat or mouse. The NOAEL for male and female rats and mice is 25 ppm.

Development of Screening Level

The chronic inhalation bioassay by Malley et al. (1995) was determined to be the most appropriate study on which to base the screening level. The US EPA Benchmark Dose Software 2.1.1 was used to model the dose response data. The 10% response level was used as a point of departure. The lower 95% confidence limit on this point, called the Benchmark Dose Lowerlimit (BMDL) was used to derive the screening level as a point of departure. Table 1 shows the endpoints and dose response data used as inputs to the software.

Table 1. Incidence of Compound-Related Observations† in Male and Female Mice

	Male Rat			
Dose (ppm)→	0	25	100	350
Hepatic Focal Cystic Degeneration	17/65	24/63	28*****/63	31*****/62
Nephropathy Severe	9/61	9/62	12/62	20*/62
	Female Mice			
Dose (ppm)→	0	25	100	350
Retinal Atrophy	4/61	8/62	6/56	20*****/58
Hepatic Cell Necrosis	1/63	2/64	2/63	10*****/65

† *From Malley et al. (1995)*

** Statistically significant elevation above controls, p<0.05*

Tables 2 through 5 show the Benchmark Dose Software output data used to evaluate the goodness of fit and the 95% lower confidence limit on dose at the 10% response level for each endpoint and model.

Table 2. Hepatic Focal Cystic Degeneration Male Rat

Model Name	AIC	Chi-square	P-value	BMDL (ppm)
Gamma	337.551	2.58	0.2757	59.07
Logistic	337.909	2.92	0.2322	83.78
Multistage	337.593	0.65	0.4189	15.68
Probit	337.888	2.9	0.2345	82.59
Weibull	337.551	2.58	0.2757	59.07
Quantal-Linear	337.551	2.58	0.2757	59.07
LogLogistic	336.954	0.01	0.9188	*Null*
LogProbit	336.951	0.01	0.9331	*Null*

Table 3. Nephropathy Severe Male Rat

Model Name	AIC	Chi-square	P-value	BMDL (ppm)
Gamma	247.349	0.04	0.8376	90.90
Logistic	245.376	0.07	0.966	135.42
LogLogistic	247.345	0.04	0.8442	29.81
LogProbit	247.326	0.02	0.8906	30.75
Multistage	247.362	0.05	0.8153	48.02
Probit	245.369	0.06	0.9693	129.17
Weibull	247.351	0.04	0.8344	90.8843
Quantal-Linear	245.379	0.07	0.9646	90.671

Table 4. Hepatic Cell Necrosis Female Mice

Model Name	AIC	Chi-square	P-value	BMDL (ppm)
Gamma	107.936	0.32	0.5731	170.13
Logistic	105.883	0.28	0.8708	241.95
LogLogistic	107.932	0.31	0.5751	160.83
LogProbit	107.947	0.32	0.5692	157.31
Multistage	107.921	0.31	0.5763	148.39
Probit	105.91	0.3	0.8589	229.64
Weibull	107.931	0.31	0.5758	170.217
Quantal-Linear	106.462	0.77	0.6821	162.425

Table 5. Retinal Atrophy Female Mice

Model Name	AIC	Chi-square	P-value	BMDL (ppm)
Gamma	197.499	1.41	0.2353	79.52
Logistic	195.464	1.44	0.486	135.49
LogLogistic	197.494	1.41	0.2355	38.76
LogProbit	197.505	1.41	0.2356	41.86
Multistage	197.476	1.44	0.2297	60.78
Probit	195.514	1.49	0.4742	126.63
Weibull	197.49	1.41	0.2354	79.572
Quantal-Linear	196.051	1.95	0.3776	76.3313

In Table 2 the LogLogistic and LogProbit models did not produce a BMDL for the hepatic focal cystic degeneration in the male rat endpoint. The highest dose was removed and the model was re-run. After dropping the high dose group, the BMDLs produced were 15.69 and 37.38 ppm for LogLogistic and LogProbit, respectively (data not shown in tables).

The endpoint hepatic focal cystic degeneration in the male rat produced the lowest BMDL (i.e., 15.68 ppm) (see Table 2) and was used to derive the reference concentration (RfC). The dose was then converted to milligrams per cubic meter (mg/m^3) using the formula:

$mg/m^3 = (ppm \times MW)/24.45$
$mg/m^3 = (15.68 \times 87.14)/24.45$
$mg/m^3 = 55.88$

where, MW is the molecular weight of DMAC (87.14g).

The exposure dose was duration adjusted to continuous exposure by accounting for the 6 hrs per day, and 7 days per week exposure scenario:

Adjusted Dose = Exposure Dose x 6hrs/24hrs x 5days/7days
Adjusted Dose = 55.88 mg/m^3 x 0.25 x 0.71
Adjusted Dose = 9.92 mg/m^3

Using guidance from the US EPA (1994), the human equivalent concentration (HEC) was estimated. Since DMAC is considered either a category 2 or 3 gas, and the blood-gas partition coefficient is unknown it was assumed that the animal dose is equivalent to the human dose, therefore, the adjusted dose = HEC = 9.92 mg/m^3.

The RfC then becomes:

$RfC = (BMDL_{HEC})/UF_H \times UF_S$
$RfC = 9.92\ mg/m^3/(10 \times 10)$
$RfC = 0.0992\ mg/m^3$
$RfC = 0.1\ mg/m^3$ (rounding to 1 significant figure).

Where, UF_H = uncertainty factor of 10 for animal to human, and
UF_S = 10 for sensitive individuals.

Converting milligrams (mg) to micrograms (µg) is done by multiplying by 1000.

$RfC = 0.1 \times 1000$
$RfC = 100\ \mu g/m^3$

Pursuant to Rule 232(1)(a) the ITSL equals the RfC, therefore, the ITSL is 100 ug/mg with a 24-hr averaging time (also see Rule 232(2)(b)).

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