METHYL ETHYL KETONE

Health Advisory
Office of Drinking Water
U.S. Environmental Protection Agency

I. INTRODUCTION

The Health Advisory (HA) Program, sponsored by the Office of Drinking Water (ODW), provides information on the health effects, analytical methodology and treatment technology that would be useful in dealing with the contamination of drinking water. Health Advisories describe nonregulatory concentrations of drinking water contaminants at which adverse health effects would not be anticipated to occur over specific exposure durations. Health Advisories contain a margin of safety to protect sensitive members of the population.

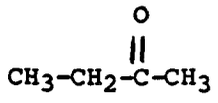
Health Advisories serve as informal technical guidance to assist Federal, State and local officials responsible for protecting public health when emergency spills or contamination situations occur. They are not to be construed as legally enforceable Federal standards. The HAs are subject to change as new information becomes available.

Health Advisories are developed for One-day, Ten-day, Longer-term (approximately 7 years, or 10% of an individual's lifetime) and Lifetime exposures based on data describing noncarcinogenic end points of toxicity. Health Advisories do not quantitatively incorporate any potential carcinogenic risk from such exposure. For those substances that are known or probable human carcinogens, according to the Agency classification scheme (Group A or B), Lifetime HAs are not recommended. The chemical concentration values for Group A or B carcinogens are correlated with carcinogenic risk estimates by employing a cancer potency (unit risk) value together with assumptions for lifetime exposure and the consumption of drinking water. The cancer unit risk is usually derived from the linear multistage model with 95% upper confidence limits. This provides a low-dose estimate of cancer risk to humans that is considered unlikely to pose a carcinogenic risk in excess of the stated values. Excess cancer risk estimates may also be calculated using the One-hit, Weibull, Logit or Probit models. There is no current understanding of the biological mechanisms involved in cancer to suggest that any one of these models is able to predict risk more accurately than another. Because each model is based on differing assumptions, the estimates that are derived can differ by several orders of magnitude.

II. GENERAL INFORMATION AND PROPERTIES

CAS No. 78-93-3

Structural Formula



Synonyms

2-Butanone, butan-2-one, ethyl methyl ketone, MEK.

Uses

- As a solvent in processes involving gums, resins, cellulose acetate, and cellulose nitrate
- Used extensively in the synthetic rubber industry
- In production of paraffin wax and high grade lubricating oil
- In household products such as surface coating compounds (lacquer and varnishes), paint remover, and glues.

Properties

Chemical Formula	C_4H_8O
Molecular Weight	72.10
Physical State	liquid
Boiling Point	79.6°C
Melting Point	--
Density	--
Vapor Pessure	100 mm Hg at 25°C
Water Solubility	295 mg/L at 25°C
Log Octanol/Water Partition Coeffficient	--
Taste Threshold	--
Odor Threshold	--
Conversion Factor	1 ppm = 2.95 mg/m_3

Occurrence

- Methyl ethyl ketone (MEK) is a synthetic organic chemical which does not occur naturally. Production of MEK in 1980 was approximately 600 million lbs (U.S. ITC, 1981).
- No information on the environmental fate of MEK has been identified. Based upon its reported vapor pressure and solublity, MEK is expected to slowly volatilize from soil and water. Due to MEK's relatively high solublity in water MEK is expected to be mobile in soil.

- MEK has not been included in Federal and State surveys of drinking water. However, a number of studies have reported that MEK does occur in surface water systems (Scheiman et al., 1974; U.S. EPA, 1976; Coleman et al., 1976).

III. PHARMACOKINETICS

Absorption

- Munies and Wurster (1965) studied the dermal absorption of MEK in humans under normal, hydrated and dehydrated skin conditions. MEK was applied at 100 ml to the forearm using an absorption cell; the duration of exposure was 8 hours. MEK was detected in the expired air at 3.6 mg/L 15 minutes after exposure. A steady-state level of 6.5 to 6.6 mg/L in the expired air was attained within 2 to 3 hours after exposure.

- DiVincenzo and coworkers (1974) reported that levels of 11% of administered MEK and metabolites were found in the serum 1 hour following a single intraperitoneal dose of 450 mg/kg in guinea pigs.

Distribution

- Dietz and Traiger (1979) determined the blood concentrations of 2-butanol, 2,3-butanediol and 3-hydroxy-2-butanone in rats after a single oral dose of 355 mg/kg MEK. The blood concentrations of MEK and metabolites 4 hours after dosing were as follows: MEK (94.1 mg/100 ml), 2-butanol (3.2 mg/100 ml), 3-hydroxy-2-butanone (2.4 mg/100 ml), and 2,3-butanediol (8.6 mg/100 ml).

Metabolism

- No information was found in the available literature on the metabolism of methyl ethyl ketone.

Excretion

- Insufficient pharmacokinetic data for MEK are available to assess distribution and elimination of MEK in animals.

IV. HEALTH EFFECTS

Humans

- Data regarding the effects of oral exposure to MEK on humans were not located in the available literature. However, Smith and Mayers (1944) reported that two young women exhibited signs of severe intoxication, including convulsions and loss of consciousness, after exposure to MEK and acetone (298 to 560 and 330 to 495 ppm, respectively).

Animals

Short-term Exposure

- The acute LD_{50} and LD_{50} of MEK have been determined for several routes of exposure:

Species	Route	LD_{50}	Reference
rat	oral	2.9 g/kg	Kimura et al., 1971
rat	inhalation	5.9 g/m^3 (2,000 ppm/4 hr)	Carpenter et al., 1949
rabbit	dermal	>8 g/kg	Smyth et al., 1962

- Kimura and co-workers (1971) also have determined the oral LD_{50} values for weanling and newborn rats to be 2.5 and 0.8 g/kg, respectively.

- Patty and co-workers (1935) studied the toxic effects of MEK inhalation in the guinea pig. The animals were exposed to high concentrations of vapor: 3,300 ppm (9.7 g/m^3), 10,000 ppm (29.5 g/m^3), 33,000 ppm (97.3 g/m^3) or 100,000 ppm (295 g/m^3) for various durations up to 14 hours. Pathologic examination was done on animals that died during exposure, on those immediately sacrificed after exposure and on animals sacrificed 4 and 8 days after termination of exposure. At levels of 10,000 ppm (29.5 g/m^3), 33,000 ppm (97.3 g/m^3) and 100,000 ppm (295 g/m^3), MEK exposure produced irritation of the nose and eyes, tearing, respiratory distress, incoordination and narcosis. Exposure to MEK vapor at a concentration of 100,000 ppm (295 g/m^3) to guinea pigs for 30 minutes or more resulted in corneal opacity. This condition improved gradually in guinea pigs that lived 4 and 8 days following exposure; at the end of 8 days, the eyes were nearly normal. This condition was not observed in animals exposed to lower concentrations. The pathologic findings in animals that died during exposure or were sacrificed immediately after exposure to MEK (at all levels except 3,300 ppm) were congestion of the liver, kidney, lung and brain congestion and emphysema. Congestion of the visceral organs was not observed in the animals sacrificed 4 and 8 days after termination of MEK exposure.

- Studies have assessed the hepatotoxic effect of MEK after acute exposure (DiVincenzo and Krasavage, 1974). Guinea pigs were administered a single intraperitoneal dose of MEK (750, 1,500 or 2,000 mg/kg). Twenty-four hours after exposure, blood samples of animals were analyzed for ornithine carbamyl transferase (OCT) activity and liver tissues were examined for histopathological changes. Liver effects observed were increased lipid content and elevated serum ornithine carbamyl transferase activity, a sensitive enzymatic assay for liver injury (Davidsohn and Wells, 1965). Elevated serum OCT activity was observed 24 hours after administration of 2,000 mg/kg of MEK. Lipid accumulation in cells of the animal was present at the two higher doses (1,500 and 2,000 mg/kg).

Long-term Exposure

- LaBelle and Brieger (1955) compared the longer-term exposure of composite solvent, containing 235 ppm (0.693 g/m^3) MEK and seven other solvents (total of 226 ppm) to MEK alone. In each case, 25 rats were exposed to the composite solvent vapors, MEK vapors or air alone for 7 hours per day, 5 days per week for 12 weeks. There were no deaths or sign of toxicity observed in the animals. There were also no significant gross or microscopic pathological changes observed at autopsy upon examination of control or exposed animals.

- Cavender et al. (1983) exposed rats of both sexes to methyl ethyl ketone at concentrations of 0, 1,250, 2,500 or 5,000 ppm, 6 hours/day, 5 days/week, for 90 days. No animals died during the study. The 90-day exposures had no adverse effect on the clinical health or growth of male or female rats except for a depression of mean body weight in the 5,000 ppm exposure group. However, at necropsy, increases in liver weight were noted in the 1,250 and 2,500 ppm group of female rats. Increases in liver weight, liver weight/body weight ratios and liver weight/brain weight ratios were observed in both male and female rats at the dose level of 5,000 ppm methyl ethyl ketone. In the male rats at the dose level of 5,000 ppm, kidney weight/body weight ratios also were elevated. Spleen and brain weights, and brain weight/body weight ratios were elevated in the 5,000 ppm female rats. Urine volumes in the 5,000 ppm male rats were higher than control values. Mean corpuscular hemoglobin values in male and female rats at the dose level of 5,000 ppm were elevated. Serum glutamic-pyruvic transaminase activity in female rats at the dose level of 2,500 ppm of MEK was elevated while female rats at the dose level of 5,000 ppm MEK exhibited significantly decreased SGPT activity. In addition, alkaline phosphatase, potassium and glucose values for female rats at the dose level of 5,000 ppm were increased relative to controls. While some of these changes were statistically significant, they were considered incidental findings, without toxicological significance.

- Inhalation exposure of rats to methyl ethyl ketone at a level of 200 ppm, 12 hours/day, 7 days/week for 24 weeks resulted in slight neurological effects visible only at 4 months of treatment (Takeuchi et al., 1983), but exposure of rats to 1,125 ppm continuously for 5 months did not result in neuropathy (Saida et al., 1976). In both studies, only a single toxicological endpoint, either motor nerve conduction velocity, mixed nerve conduction velocities, or distal motor latency (Takeuchi et al., 1983) or paralysis (Saida et al., 1976), was examined. It was interesting to note in the study by Saida et al. (1976) that rats exposed to the combination of methyl ethyl ketone and methyl n-butyl ketone developed paralysis after 25 days, and exposure to 225 ppm methyl n-butyl ketone alone produced paralysis after 66 days (suggesting that methyl ethyl ketone shortened the latency period for the onset of methyl n-butyl ketone-induced neuropathy.

Reproductive Effects

- Data reported by Schwetz and co-workers (1974) implicate MEK to be an embryotoxic, fetotoxic and teratogenic agent in the rat. Pregnant rats (Sprague-Dawley) were exposed to MEK vapor at a concentration of 1,126 ppm (3.3 g/m^3) or 2,618 ppm (7.7 g/m^3) for 7 hours/day on days 6 through 15 of gestation. The following parameters were evaluated: maternal mortality, liver weight and behavior, number of corpora lutea/dam, number of resorptions, number of implantations, fetal mortality, fetal weight and size, and skeletal and visceral anomalies among the fetuses. MEK exposure at either dose level did not appear to affect adversely the number of implantation sites, the number of live fetuses/litter, or the number of corpora lutea/dam. There was evidence of fetotoxicity as indicated by a marked decrease in fetal body weights following exposure to 1,126 ppm (3.3 g/m^3). Decreased fetal weight was not observed after exposure to 2,618 ppm (7.7 g/m^3) of MEK. Skeletal and visceral anomalies were noted after exposure to MEK. The total incidence of skeletal anomalies (skull, vertebral, and sternebral) was increased significantly ($P<0.05$) in the 1126 ppm exposure group compared to the controls. A significant difference ($P<0.05$) also was observed in the incidence of skeletal defects of the sternum of the high-dose group and controls. The occurrence of visceral anomalies, including dilated ureters and subcutaneous edema, was significantly ($P<0.05$) increased in the offspring of rats treated at the high level (2,618 ppm, 7.7 g/m^3).

Developmental Effects

- The results of another study of embryo- and fetotoxicity of inhaled MEK in rats were reported by Deacon and co-workers (1981). In this study, pregnant Sprague-Dawley rats were exposed to 0, 400 ppm (1.2 g/m^3), 1,000 ppm (2.9 g/m^3) or 3,000 ppm (8.8 g/m^3) MEK for 7 hours/day on days 6 through 15 of gestation. Maternal toxicity, as evidenced by decreased body weight gain and increased food consumption, was observed among rats exposed to 3,000 ppm (8.8 g/m^3); slight fetotoxicity was observed among litters of rats exposed to this level as evidenced by an increased incidence of two minor skeletal variants. The results of this study verify the observation of an increased incidence of skeletal variants observed in the earlier study by Schwetz and co-workers (1974).

Mutagenicity

- The mutagenic potential of MEK was investigated in a testing of microbial mutagenicity of pesticides (Smirasu, 1976). In this study, MEK was used as one of several solvents for the mutagenicity screening. The test systems used were Escherichia coli WP2 and Salmonella typhimurium strains TA1535, TA1537, TA1536 and TA1538 to detect base-pair substitutions and frameshift mutations. There was no increase in the number of revertants observed in any of the test systems following exposure to MEK. However, it should be noted that MEK was tested as a solvent control at a single concentration.

Carcinogenicity

- No information was found in the available literature on the carcinogenic effects of MEK exposure to humans or animals.

V. QUANTIFICATION OF TOXICOLOGICAL EFFECTS

Health Advisories (HAs) are generally determined for One-day, Ten-day, Longer-term (approximately 7 years) and Lifetime exposures if adequate data are available that identify a sensitive noncarcinogenic end point of toxicity. The HAs for noncarcinogenic toxicants are derived using the following formula:

$$HA = \frac{(NOAEL \text{ or } LOAEL) \times (BW)}{(UF) \times (\_\_\_ L/day)} = \_\_\_ mg/L \ (\_\_\_ ug/L)$$

where:

NOAEL or LOAEL = No- or Lowest-Observed-Adverse-Effect-Level in mg/kg bw/day.

BW = assumed body weight of a child (10 kg) or an adult (70 kg).

UF = uncertainty factor (10, 100 or 1,000), in accordance with NAS/ODW guidelines.

___ L/day = assumed daily water consumption of a child (1 L/day) or an adult (2 L/day).

One-day Health Advisory

A One-day HA for MEK is calculated based upon findings reported by DiVincenzo and Krasavage (1974). Guinea pigs were administered MEK at a single intraperitoneal dose of 750, 1,500 or 2,000 mg/kg. Hepatotoxicity in guinea pigs was measured in terms of increased serum ornithine carbamyl transferase activity and lipid accumulation in the liver. Elevated serum ornithine carbamyl transferase activity was observed 24 hours after administration of 2,000 mg/kg of MEK. Lipid accumulation in liver cells of animals was noted also at the two higher doses (1,500 and 2,000 mg/kg). Therefore, in view of demonstrated hepatotoxicity in terms of increased serum enzyme activity (at dose level of 2,000 mg/kg) and lipid accumulation in the liver cells at dose levels of 1,500 and 2,000 mg/kg of MEK, the lowest dose level, 750 mg/kg as the NOAEL will be used in the development of a One-day HA.

The One-day HA for a 10 kg child is calculated as follows:

$$\text{One-day HA} = \frac{(750 \text{ mg/kg day})(10 \text{ kg})}{(100)(1 \text{ L/day})} = 75 \text{ mg/L} = 75000 \text{ ug/L}$$

where:

750 mg/kg day = NOAEL based on absence of increase in enzyme activity in guinea pigs.

10 kg = assumed body weight of a child.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

1 L/day = assumed daily water consumption of a child.

Ten-day Health Advisory

There are no data from which to derive a Ten-day HA directly. Therefore, it is recommended that the HA can be determined by dividing the One-day HA by 10, resulting in a HA of 7500 ug/L for a 10 kg child.

Longer-term Health Advisory

Adequate duration-specific oral data are not available from which to derive the Longer-term HA. However, the LaBelle and Brieger (1955) inhalation study in rats may be considered for a longer-term HA. In this study, a group of 25 rats was exposed to 235 ppm (693 mg/m^3) MEK for 7 hours/day, 5 days/week for 12 weeks. Without indicating the specific organs examined, the authors reported that no significant pathological changes were observed either macroscopically or microscopically. The Longer-term HA is derived as follows:

Step 1: Determination of the Total Absorbed Dose (TAD)

$$TAD = \frac{(693\ mg/m^3)(1\ m^3/hr)(7\ hr/day)(5/7)(0.5)}{70\ kg} = 24.7\ mg/kg/day$$

where:

693 mg/m^3 = NOAEL of 235 ppm based on absence of pathological change in rats.

1 m^3/hr = respiratory rate of adult human (pulmonary rate/body weight ratio) assumed to be the same for humans and test animals.

7 hr/day = exposure duration.

5/7 = conversion from 5 days exposure to 7 days exposure.

0.5 = assumed fraction of MEK absorbed.

70 kg = assumed body weight of an adult.

Step 2: Determination of the Longer-Term HA

Longer-term HA for a 10-kg child:

$$\frac{(24.7\ mg/kg/day)\ (10\ kg)}{(100)\ (1\ L/day)} = 2.5\ mg/L\ (or\ 2500\ ug/L)$$

where:

24.7 mg/kg/day = TAD.

10 kg = assumed body weight of a child.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

1 L/day = assumed daily water consumption of a child.

Longer-term HA for a 70-kg adult:

$$\frac{(24.7 \text{ mg/kg/day})\ (70 \text{ kg})}{(100)\ (2 \text{ L/day})} = 8.6 \text{ mg/L (or 8600 ug/L)}$$

where:

24.7 mg/kg/day = TAD.

70 kg = assumed body weight of an adult.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

2 L/day = assumed daily water consumption of an adult.

Lifetime Health Advisory

The Lifetime HA represents that portion of an individual's total exposure that is attributed to drinking water and is considered protective of noncarcinogenic adverse health effects over a lifetime exposure. The Lifetime HA is derived in a three step process. Step 1 determines the Reference Dose (RfD), formerly called the Acceptable Daily Intake (ADI). The RfD is an estimate of a daily exposure to the human population that is likely to be without appreciable risk of deleterious effects over a lifetime, and is derived from the NOAEL (or LOAEL), identified from a chronic (or subchronic) study, divided by an uncertainty factor(s). From the RfD, a Drinking Water Equivalent Level (DWEL) can be determined (Step 2). A DWEL is a medium-specific (i.e., drinking water) lifetime exposure level, assuming 100% exposure from that medium, at which adverse, noncarcinogenic health effects would not be expected to occur. The DWEL is derived from the multiplication of the RfD by the assumed body weight of an adult and divided by the assumed daily water consumption of an adult. The Lifetime HA is determined in Step 3 by factoring in other sources of exposure, the relative source contribution (RSC). The RSC from drinking water is based on actual exposure data or, if data are not available, a value of 20% is assumed for synthetic organic chemicals and a value of 10% is assumed for inorganic chemicals. If the contaminant is classified as a Group A or B carcinogen, according to the Agency's classification scheme of carcinogenic potential (U.S. EPA, 1986), then caution should be exercised in assessing the risks associated with lifetime exposure to this chemical.

Lifetime HA for MEK may be derived based on LaBelle and Brieger (1955) inhalation study in rats for 12 weeks. In this study, a NOAEL of 693 mg/m^3

was identified. Animals were exposed to MEK for 7 hours/day, 5 days/week for 12 weeks. The Lifetime HA is derived as follows:

Total absorbed dose (TAD) of 24.7 mg/kg/day was determined as described under Longer-term HA.

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{24.7 \text{ mg/kg/day}}{(1,000)} = 0.0247 \text{ mg/kg/day}$$

where:

24.7 mg/kg/day = TAD (NOAEL) based on absence of pathological changes.

1,000 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study of less-than-lifetime duration.

Step 2: Determination of the Drinking Water Equivalent Level (DWEL)

$$DWEL = \frac{(0.0247 \text{ mg/kg/day}) (70 \text{ kg})}{2 \text{ L/day}} = 0.86 \text{ mg/L or } 860 \text{ ug/L}$$

where:

0.0247 mg/kg/day = RfD.

70 kg = assumed body weight of an adult.

2 L/day = assumed daily water consumption of an adult.

Step 3: Determination of the Lifetime Health Advisory

Lifetime HA = 0.86 mg/L x 20% = 0.17 mg/L (170 ug/L)

where:

0.86 mg/L = DWEL.

20% = assumed relative source contribution from water.

Evaluation of Carcinogenic Potential

- No studies on the carcinogenic effects in animals to MEK have been found in the available literature.
- IARC has not made an assessment of MEK's carcinogenic potential.
- Applying the criteria described in EPA's guidelines for assessment of carcinogenic risk (U.S. EPA, 1986), methyl ethyl ketone may be

classified in Group D: Not classified. This category is for agents with inadequate animal evidence of carcinogenicity.

VI. OTHER CRITERIA, GUIDELINES AND STANDARDS

- An occupational threshold limit value (TLV) of 200 ppm was set by ACGIH (1980).

VII. ANALYTICAL METHODS

- There is no standardized method for the determination of methyl ethyl ketone in drinking water samples. However, methyl ethyl ketone may be determined by purge and trap gas chromatographic-mass spectrometric (GC-MS) procedure used for determination of volatile organic compounds in industrial and municipal discharges (U.S. EPA, 1984). In this method, a 5 mL water sample is spiked with an internal standard of an isotopically stable analog of methyl ethyl ketone and purged with an inert gas. The volatile compounds are transferred from the aqueous phase into the gaseous phase where they are passed into a sorbent column and trapped. After purging is completed, the trap is backflushed and heated to desorb the compounds on to a gas chromatograph (GC). The compounds are separated by the GC and detected by a mass spectrometer (MS). The labeled compound serves to correct the variability of the analytical technique. The method detection limit is dependent upon the nature of interferences, but it is estimated to be 50 ug/L.

VIII. TREATMENT TECHNOLOGIES

- Because of its polarity and resulting miscibility in water, MEK is a difficult compound to remove from contaminated potable water. The conventional water treatment techniques of coagulation and sand filtration are ineffective in MEK removal (McGuire et al., 1978).

- Chlorination does cause some oxidative degradation of MEK. Treatment with 100 mg/L chlorine for 12 hours reduced MEK by 5% (McGuire et al., 1978). However, such treatment leads to the formation of trihalomethanol which makes chlorination an undesirable treatment. Oxidative treatment with 100 mg/L potassium permanganate for 3 hours was completely ineffective in reducing MEK concentrations (McGuire, 1978).
- MEK also is not a good candidate for removal by air stripping. It has a low Henry's Law Constant of 3.4×10^{-5} atm m^3/mole (McGuire et al., 1978).

- Adsorption to granular activated carbon (GAC) offers the best potential for MEK removal. McGuire et al. (1978) reported a 95% removal efficiency using a 1.1 min detention time over a 1.2 hr treatment period. However, in another laboratory investigation of removal of MEK (7.2 mg/L) by Filtrasorb 400, breakthrough occurred after 3 hours of treatment at a flow rate of 23 ml/min and a detention time of 2.1 min (McGuire et al., 1978).

- McGuire et al. (1978) also attempted laboratory isotherm studies using GAC and 0.2 mm ortho-phosphate buffered glass distilled water as a solvent for the MEK. These results also indicate that treatment with GAC can be used to remove MEK.

- Treatment with powdered activated carbon (PAC) however, does not seem to be as effective (McGuire et al., 1978; Kuo et al., 1977).

- Treatment technologies for the removal of methyl ethyl ketone from water are available and have been reported to be effective. Selection of individual or combinations of technologies to achieve methyl ethyl ketone reduction must be based on a case-by-case technical evaluation, and an assessment of the economics involved.

- Positioning the chlorination step in water treatment so that it occurs after MEK removal also should be considered since MEK can serve as a precursor for THM formation.

IX. REFERENCES

ACGIH. 1980. American Conference of Governmental Industrial Hygienists. TLVs - Threshold limit values for chemical substances in workroom air, adopted by ACGIH for 1980. Cincinnati, OH.

Carpenter, C.P., H.F. Smyth and U.C. Pozzani. 1949. The assay of acute vapor toxicity, and the grading and interpretation of results on 96 chemical compounds. J. Ind. Hyg. Tox. 31(6):343-346.

Cavender, F.L., H.W. Casey, H. Salem, J.A. Swenberg and E.J. Gralla. 1983. A 90-day vapor inhalation toxicity study of methyl ethyl ketone. Fund. Appl. Toxicol. 3:264-270.

Chain, E.S.K. 1982. Oxidation of particular organics. Personal communication.

Coleman, W.E., R.D. Lingg, R.G. Melton and F.C. Kopfler. 1976. The occurrence of volatile organics in five drinking water supplies using gas chromatography/mass spectrometry. Chapter 21. In: L.H. Keith, ed. Identification and analysis of organic pollutants in water. Ann Arbor, MI: Ann Arbor Science Publications, Inc.

Deacon, M.M., M.D. Pilny, J.A. John, B.A. Schwetz, F.J. Murray, H.O. Yakel and R.A. Kuna. 1981. Embryo- and fetotoxicity of inhaled methyl ethyl ketone in rats. Toxicol. Appl. Pharmacol. 59:617-619.

Dietz, F.K., and G.J. Traiger. 1979. Potentiation of CCL_4 of hepatotoxicity in rats by a metabolite of 2-butanone: 2,3-butanediol. Toxicology. 14:209-215.

DiVincenzo, G.D., and N.J. Krasavage. 1974. Serum ornithine carbamyl transferase as a liver response test for exposure to organic solvents. Am. Ind. Hyg. Assoc. J. 35:21-29.

Duckett, S., N. Williams and S. Francis. 1974. Peripheral neuropathy associated with inhalation of methyl n-butyl ketone. Experientia. 30:1283.

Hites, R.A., G.A. Jungclaus, V. Lopez-Avila and L.S. Sheldon. 1979. Potentially toxic organic compounds in industrial wastewater and river systems: two case studies. ACS Symp. Ser. 94:63-90. D. Schuetzle, ed., Monitoring Toxic Substances.

Kimura, E.T., D.E. Ebert and P.W. Dodge. 1971. Acute toxicity and limits of solvent residue for sixteen organic solvents. Toxicol. Appl. Pharmacol. 19:699-704.

Kuo, P.P.K., E.S.K. Chain, F.B. DeWalle and J.H. Kim. 1977. Gas stripping, sorption, and thermal desorption procedures for preconcentrating volatile polar water-soluble organics from water samples for analysis by gas chromatography. Analytical Chemistry. 6:1023-1029.

LaBelle, C.W., and H. Brieger. 1955. The vapor toxicity of a composite solvent and its principal components. Arch. Ind. Health. 12:623-627.

Love, O.T., and R.G. Eilers. 1981. Treatment for the control of trichloroethylene and related industrial solvents in drinking water. U.S. Environmental Protection Agency, Drinking Water Research Division. Cincinnati, Ohio.

McGuire, M.J., I.H. Suffet and J.V. Radziul. 1978. Assessment of unit processes for the removal of trace organic compounds from drinking water. JAWWA. 10:565-572.

Munies, R., and D.E. Wurster. 1965. Investigation of some factors influencing percutaneous absorption. Absorption of methyl ethyl ketone. J. Pharm. Sci. 54:1281-1284.

NIOSH. 1980. National Institute for Occupational Safety and Health. 2-Butanone (MEK). In: Quarterly hazard summary report. Cincinnati, OH: National Institute for Occupational Safety and Health.

Patty, F.A., H.H. Schrink and W.P. Yant. 1935. Acute response of guinea pigs to vapors of some new commercial organic compounds. U.S. Public Health Reports. Vol. 50, pp. 1217-1228.

Saida, K., J.R. Mendell and H.S. Weiss. 1976. Peripheral nerve changes induced by methyl n-butyl ketone and potentiation by methyl ethyl ketone. J. Neuropath. Exp. Neurol. 35(3):207-225.

Scheiman, M.A., R.A. Saunders and F.E. Sallfeld. 1974. Organic contaminants of the District of Columbia water supply. BioMedical Mass Spectrometry. Vol. 1. pp 209.

Schwetz, B.A., B.K.J. Leong and P.J. Gehring. 1974. Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in rats. Toxicol. Appl. Pharmacol. 28:452-464.

Shackelford, W., and L.H. Keith. 1976. Frequency of organic compounds identified in water. Athens, GA: U.S. Environmental Protection Agency, Environmental Research Laboratory. (EPA-600/4-76-062)

Singley, J.E., and L.J. Bilello. 1981. Advances in the development of design criteria for packed column aeration. Submitted to Journal AWWA, 1981.

Smirasu, Y. 1976. Mutagenicity testing of pesticides. Kogia to Taisaku. J. Environ. Pollu. Control. 12:407-412.

Smith, A.R., and M.R. Mayers. 1944. Poisoning and fire hazards of butanone and acetone. Indust. Hyg. Bull., New York State Dept. Labor. 23:174. (Cited in LaBelle, C.W., and Brieger, H., 1955 paper)

Smyth, H.F., C.P. Carpenter, C.S. Weil, U.O. Pozzani and J.A. Striegel. 1962. Range-finding toxicity data: List VI. Am. Ind. Hyg. Assoc. J. 23:95-107.

Spencer, P.S., and H.H. Schaumburg. 1976. Feline nervous system response to chronic intoxication with commercial grades of methyl n-butyl ketone, methyl iso-butyl ketone, methyl ethyl ketone. Toxicol. Appl. Pharmacol. 30:301-311.

Takeuchi, Y., Y. Ono, N. Hisanga, M. Iwata, M. Aoyama, J. Kitoh, and Y. Sugiura. 1983. An experimental study of the combined effects of n-hexane and methyl ethyl ketone. Brit. J. Ind. Med. 40:199-203.

Traiger, G.J., and J.V. Bruckner. 1976. The participation of 2-butanone in 2-butanol-induced potentiation of carbon tetrachloride hepatotoxicity. J. Pharmacol. Exper. Therap. 196(2):493-500.

U.S. EPA. 1976. U.S. Environmental Protection Agency. Frequency of organic compounds identified in water. Environmental Research Lab, Athens, GA., PB-265 470.

U.S. EPA. 1984. U.S. Environmental Protection Agency. Method 1624 Revision B. Volatile Organic Compounds by Isotope Dilution GC/MS. Federal Register. 49(209):433407-433415, October 26.

U.S. EPA. 1986. U.S. Environmental Protection Agency. Final guidelines for carcinogen risk assessment. Federal Register. 51(185) 33992-34003. September 24.

U.S. ITC. 1981. United States International Trade Commission. Synthetic organic chemicals United States production. USITC Publication 1183. Washington, D.C. 20436.

Wang, T.C., and J.C. Bricker. 1979. 2-Butanone and tetrahydrofuran contamination in the water supply. Bull. Environ. Contam. Toxicol. 23:620-623.

Windholz, M., ed. 1976. The Merck Index, 9th ed. Merck and Co., Inc. Rahway, N.J. p. 5937.

Zakhari, S., P. Levy, M. Leibowitz and D.M. Aviado. 1977. Review of the literature on methyl ethyl ketone. In: Isopropanol and ketones in the environment. Cleveland, OH: CRC Press, Inc.