

natural products and may be a minor product of normal mammalian metabolism. In 1999, U.S. production capacity was 675 million pounds.

The inhalation toxicity of MEK is low. Low concentrations are only mildly irritating. At high concentrations MEK causes a narcotic effect on the central nervous system as evidenced by neurobehavioral effects in animals. MEK is not teratogenic, but at high concentrations is mildly fetotoxic to rats and mice. Data on human exposures were available from clinical studies and workplace monitoring. Animal studies with a variety of species (baboon, rat, mouse, and guinea pig) addressed irritation, neurotoxicity, developmental toxicity, chronic toxicity/carcinogenicity, and lethality. Exposure durations ranged from acute to chronic. Genotoxicity was also addressed.

Two studies with human volunteers exposed to 100, 200, or 350 ppm were evaluated for the AEGL-1; the exposure times were 5 minutes (Nelson et al. 1943) and 4 hours (Dick et al. 1992). Although a concentration of 200 ppm was judged unobjectionable in both studies, slight nose and throat irritation were noted at 100 ppm in the Nelson et al. (1943) study. Therefore, 100 ppm was selected as the threshold for sensory irritation. The safety of this value is supported by numerous clinical studies in which volunteers were routinely exposed to 200–400 ppm for up to 4 hours without reports of irritation or changes in neurobehavioral

parameters. Because this is a threshold value and slight irritation should not increase in intensity with time, an intraspecies uncertainty factor of 1 was applied. Because accommodation to slight irritation occurs, the 100 ppm concentration was used across all AEGL-1 exposure durations. Furthermore, MEK is rapidly metabolized and will not accumulate in the blood or in the body which further supports using the same value for all the time intervals.

The AEGL-2 was based on the chronic study of Cavender et al. (1983) in which rats were exposed to 5,000 ppm for 5 days/week for 90 days. No lesions were reported in this study, but the concentration is close to the threshold for neurotoxicity as evidenced by somnolence in another repeated exposure study in which rats were exposed to 6,000 ppm for several weeks (Altenkirch et al. 1978). Because this was a no-effect repeated-exposure study, no interspecies uncertainty factor was applied. Because the threshold for narcosis differs by no more than 2- to 3-fold among the general population, an intraspecies uncertainty factor of 3 was applied to protect sensitive individuals. Because the threshold for narcosis is concentration dependent, the resulting 1,700 ppm concentration was applied across all AEGL-2 exposure durations.

The AEGL-3 values were based on two different studies. The 10- and 30-minute values were based on a study with mice in which a 30-minute

exposure to 31,426 ppm was projected to reduce the respiratory rate by 50%; there were no deaths at the highest tested concentration of 26,416 ppm (Hansen et al. 1992). Because a 30-minute exposure of rats to 3 times this concentration (92,239 ppm) also resulted in no deaths (Klimisch 1988), the 31,426 ppm value was adjusted by an interspecies uncertainty factor of 1. Because the threshold for narcosis differs by no more than 2- to 3-fold among the general population, an intraspecies uncertainty factor of 3 was applied to protect sensitive individuals. The resulting value of 10,000 ppm was used for the 10-minute and 30-minute AEGL-3 exposure durations. The longer-term values were based on an MLE₀₁ of 7,500 ppm calculated by Fowles et al. (1999) from a 4-hour study with rats exposed to several concentrations for 4 hours (La Belle and Brieger 1955). In this study the 4-hour LC₅₀ was 11,700 ppm and the highest concentration resulting in no deaths was 7,850 ppm for 4 hours. The 7,500 ppm concentration was divided by an intraspecies uncertainty factor of 3. The resulting value of 2,500 ppm was used for both the 4-hour and 8-hour AEGL-3 values because MEK would reach equilibrium in the body prior to this time period. The 4-hour 2,500 ppm value was time scaled to the 1 hour time using the default n value of 3 for scaling to shorter time intervals.

The proposed AEGL values are listed in Table 8 of this unit.

TABLE 8.—SUMMARY OF PROPOSED AEGL VALUES FOR METHYL ETHYL KETONE [PPM (MG/M³)]

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1 (Nondisabling)	100 (293)	100 (293)	100 (293)	100 (293)	100 (293)	Threshold for sensory irritation in humans (Nelson et al. 1943)
AEGL-2 (Disabling)	1,700 (4,980)	1,700 (4,980)	1,700 (4,980)	1,700 (4,980)	1,700 (4,980)	Threshold for narcosis— rats (Cavender et al. 1983)
AEGL-3 (Lethal)	10,000 ^{a,b} (29,300)	10,000 (29,300)	4,000 ^c (11,720)	2,500 (7,325)	2,500 (7,325)	Threshold for lethality— mouse (Hansen et al. 1992; La Belle and Brieger 1955)

^aBased on Hansen et al. (1992).

^bThis value is more than one-half of the lower explosive limit of 18,000 ppm.

^cBased on La Belle and Brieger (1955).

ii. *References.* a. Altenkirch, H.; G. Stoltenburg; and H.M. Wagner. 1978. Experimental studies on hydrocarbon neuropathies induced by methyl-ethyl-ketone (MEK). *Journal of Neurology*. 219:159–170.

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