

TABLE 1.—10 CHEMICALS FOR PROPOSED AEGLS—Continued

CAS No.	Chemical name
1330–20–7	Xylenes

*B. Executive Summaries*

The following are executive summaries from the chemical specific technical support documents (which may be obtained as described in Unit I.B. and III.) that support the NAC/AEGL Committee's development of AEGL values for each chemical substance. This information provides the following information: A general description of each chemical, including its properties and principle uses; a summary of the rationale supporting the AEGL-1, 2, and 3 concentration levels; a summary table of the AEGL values; and a listing of key references that were used to develop the AEGL values. More extensive toxicological information and additional references for each chemical may be found in the complete technical support documents. Risk managers may be interested to review the complete technical support document for a chemical when deciding issues related to use of the AEGL values within various programs.

1. *Acetone cyanohydrin*—i.

**Description.** Acetone cyanohydrin is a colorless to yellowish liquid with a characteristic bitter almond odor due to the presence of free HCN. The major use of acetone cyanohydrin is in the production of  $\alpha$ -methacrylic acid and its esters; the latter are used for the production of plexiglass. Further uses of acetone cyanohydrin are in the production of acrylic esters, polyacrylic plastics, and synthetic resins as well as in the manufacture of insecticides, pharmaceuticals, fragrances, and perfumes. Acetone cyanohydrin decomposes spontaneously to acetone and hydrogen cyanide; this process is catalyzed by heat and contact with water (especially under alkaline conditions).

Fatal cases and life-threatening poisonings in workers have been described after accidental inhalation, skin contact, and oral uptake. Initial symptoms following mild exposure to acetone cyanohydrin are predominantly cardiac palpitation, headache, weakness, dizziness, nausea, vomiting, and nose, eye, throat, and skin irritation. The systemic toxicity of acetone cyanohydrin is caused by free cyanide ions and is primarily due to complex formation with the iron moiety in the tissue enzyme ferri cytochrome c oxidase or cytochrome  $a_3$ . The blockage

of the electron transport system of mitochondria results in inhibition of oxygen utilization and causes tissue hypoxia and cellular and tissue destruction.

Four studies exposed rats repeatedly to acetone cyanohydrin concentrations of about 10, 30, and 60 ppm for 6 hours/day, 5 days/week for a total of 4 weeks (Monsanto Co., 1986a; using groups of 10 male and 10 female rats), 10 weeks (Monsanto Co., 1982b; using groups of 15 male rats) and 14 weeks (Monsanto Co., 1986b; using groups of 15 male and 15 female rats) or for 6 hours/day for 21 days (Monsanto Co., 1982c; using groups of 15 female rats). Death was observed at 60 ppm after the first exposure in 3 animals of the Monsanto Co. (1986a) study, but not in subsequent exposures or in the other studies at a similar exposure concentration. Preceding death, respiratory distress, prostration, convulsions, and tremors were observed. In all studies, exposure to 60 and 30 ppm caused signs of irritation (red nasal discharge, clear nasal discharge, perioral wetness, encrustations) during the first and subsequent weeks of exposure. At 10 ppm, red nasal discharge was not observed in one study (Monsanto Co., 1986a); its incidence was not increased compared to control group in two studies (Monsanto Co., 1982b; 1982c) and increased compared to the control group in the fourth study (Monsanto Co., 1986b). No other effects were reported in these four studies.

The AEGL-1 was based on a repeated exposure study in rats in which a concentration of 9.2 ppm for 6 hours/day, 5 days/week for 4 weeks did not result in red nasal discharge (Monsanto Co., 1986a). An uncertainty factor of 3 was applied for interspecies variability because the lowest-observed-effect-level (LOEL) for irritation in humans exposed to cyanide at the workplace is about 6–10 ppm cyanide (El Ghawabi et al., 1975), which is a factor of about 3 below the irritation threshold of acetone cyanohydrin in rats (about 30 ppm) and because a multiple exposure study was used for the derivation of AEGL values. An uncertainty factor of 3 was applied for intraspecies variability because decomposition of acetone cyanohydrin does not involve enzyme-catalyzed steps and the binding to evolutionary conservative iron-containing proteins/enzymes, i.e., the target protein cytochrome c oxidase, is unlikely to differ substantially between individuals. A modifying factor of 2 was applied due to the lack of more adequate and supporting data for the derivation of AEGL-1 values. The exposure duration-specific values were derived by time

scaling according to the dose-response regression equation  $C^n \times t = k$ , using the default of  $n = 3$  for shorter exposure periods and  $n = 1$  for longer exposure periods, due to the lack of suitable experimental data for deriving the concentration exponent. For the 10-minute AEGL-1 the 30-minute value was applied because the derivation of AEGL values was based on a long experimental exposure period and no supporting studies using short-exposure periods were available for characterizing the concentration-time-response relationship.

The AEGL-2 was based on a repeated exposure study in rats in which a concentration of 29.9 ppm for 6 hours/day, 5 days/week for 4 weeks did not result in respiratory distress (red nasal discharge as a sign of irritation was observed during the first and subsequent weeks of exposure) (Monsanto Co., 1986a). An uncertainty factor of 3 was applied for interspecies variability because repeated exposure of humans at the workplace to cyanide concentrations only about 3-fold lower than the lethality threshold of about 60 ppm acetone cyanohydrin in rats did not lead to life-threatening or irreversible health effects and because a multiple exposure study was used for the derivation of AEGL values. An uncertainty factor of 3 was applied for intraspecies variability because decomposition of acetone cyanohydrin does not involve enzyme-catalyzed steps and the binding to evolutionary conservative iron-containing proteins/enzymes, i.e., the target protein cytochrome c oxidase, is unlikely to differ substantially between individuals. The exposure duration-specific values were derived by time scaling according to the dose-response regression equation  $C^n \times t = k$ , using the default of  $n = 3$  for shorter exposure periods and  $n = 1$  for longer exposure periods, due to the lack of suitable experimental data for deriving the concentration exponent. For the 10-minute AEGL-2 the 30-minute value was applied because the derivation of AEGL values was based on a long experimental exposure period and no supporting studies using short-exposure periods were available for characterizing the concentration-time-response relationship.

For the derivation of AEGL-3 values, it was taken into account that:

a. Acetone cyanohydrin decomposes spontaneously into hydrogen cyanide and acetone,

b. The decomposition of acetone cyanohydrin is accelerated by heat and water,