

exposures. Comparative data for the same exposure duration show that mice are more sensitive than rats to the acute toxic effects of ammonia (10 minute LC₅₀ values for mice and rats, are 10,096 ppm and 40,300 ppm, respectively). The lowest lethal concentrations reported was 1,000 ppm for the cat. However, cats were exposed via an endotracheal tube, which probably exacerbated the effects in the tracheobronchial region by bypassing the scrubbing action of the nasopharyngeal region. Rats exposed by inhalation to lethal concentrations of ammonia, showed signs of dyspnea, irritation to the eyes and nose, and hemorrhage in the lungs. Mice exposed to lethal concentrations of ammonia showed signs of irritation to the eyes and nose, along with tremors, ataxia, convulsions, seizures, and pathologic lesions in the alveoli. Cats exposed to the lowest lethal concentration showed evidence of severe airway damage, bronchopneumonia, bronchitis, bronchiolitis, and emphysema. Toxic effects at non-lethal concentrations in mice and rats consisted of mild effects on respiratory epithelium of the nasal cavity (mice and rats), reduction in the respiratory rate (mice), and evidence of eye irritation (rat). The RD₅₀ (concentration causing a 50% reduction in respiratory rate) for the mouse was 300 ppm for a 30-minute exposure.

The AEGL values for the three toxicity levels (nondisabling, disabling, and lethal) were derived from both human and animal data. The odor of ammonia is detected by humans at concentrations ranging from 5 to 53 ppm and data showed that it is irritating to the upper respiratory tract of humans at 30 ppm. The AEGL-1 value of 25 ppm is based the concentration slightly below the lowest concentration showing irritation in humans. An intraspecies uncertainty factor of 1 was applied, because 25 ppm is below the concentration causing irritation; however, if irritation did occur, it would be mild or only slightly noticeable, confined to the nasal cavity and eyes (ammonia is efficiently scrubbed), and would not be expected to

affect asthmatic or other sensitive individuals to a greater degree than nonasthmatic individuals. Atopic and nonatopic subjects did not respond differently to a nasal exposure to ammonia. The AEGL-1 values are based on human data; therefore, an interspecies uncertainty factor is not applicable. Because upper respiratory tract irritation at low ammonia concentrations is not expected to change or become more severe with duration of exposure, except for adaptation, the same value of 25 ppm is applied to all AEGL-1 exposure durations.

The AEGL-2 values were based on a study of nonexpert human subjects who had no previous exposure to ammonia and were not familiar with effects of ammonia. At least one of eight subjects reported nuisance or offensive irritation to the eyes and throat during exposure to 110 ppm of ammonia for 1 hour (Verberk, 1977). The effects reported were less serious than those described in the AEGL-2 definition, no residual effects were reported after termination of exposure, and pulmonary function was not affected by exposure. At the next highest concentration, some of the subjects reported the effects to be unbearable and left the chamber between 30 minutes and 1 hour. Their responses suggest that this concentration would impair escape. An intraspecies uncertainty factor of 1 was used for deriving the AEGL 2 values because the responses of the non-expert group ranged from just perceptible to offensive, but the AEGL-2 value was based on the response of the most sensitive individuals. The reported effects from this group involved primarily the upper respiratory tract and eyes and is unlikely to affect asthmatics differently from the most sensitive non-expert individuals. In addition, atopic subjects responded similarly to non-atopic subjects to a brief nasal exposure to ammonia, and exercising subjects showed only a small equivocal decrease in pulmonary function. The equation $C^n H t = k$, where $n = 2$, was used to extrapolate to 5-, 10-, and 30-minute

exposure durations. This equation was based on mouse and rat lethality data. The same AEGL-2 values were established for 1-, 4-, and 8-hour exposures, because the responses of the subjects exposed to 110 ppm of ammonia were similar after 1- and 2-hour exposures.

The AEGL-3 values were based on LC₀₁ values of 3,317 and 3,374 ppm derived by probit analysis of mouse lethality data reported by Kapeghian et al. (1982) and MacEwen and Vernot (1972), respectively. An uncertainty factor of 3 was applied to account for intraspecies variability because at high concentrations of ammonia, severe irritation is elicited immediately upon contact with the eyes and mucous membranes of the respiratory tract and the severity of effects such as pulmonary edema and damage to the tracheobronchial region would be similar in asthmatics and non-asthmatics. There is no reason to apply a larger uncertainty factor to protect individuals with asthma because the severe damage to the respiratory tract would have a greater and longer-lasting consequence than that of asthma. Another reason for not applying a larger intraspecies uncertainty factor to protect children is the evidence from one study showing that a child recovered from an accidental exposure to ammonia, whereas the mother carrying the child suffered severe permanent damage to the lungs. An interspecies uncertainty factor of 1 was applied to the mouse data, because the mouse was the most sensitive species among mammals. In addition, applying a larger uncertainty factor would result in a 30-minute AEGL-3 value less than the 500 ppm that human can tolerate for 30 minutes without lethal or long-term consequences. The equation, $C^n H t = k$ (where $n = 2$) based on mouse lethality data, was used to extrapolate to different exposure durations.

The proposed AEGL values are listed in Table 3 of this unit.

TABLE 3.—SUMMARY OF PROPOSED AEGL VALUES FOR AMMONIA [PPM (MG/M³)]

Classification	Exposure duration						Endpoint (Reference)
	5-minutes	10-minutes	30-minutes	1-hour	4-hours	8-hours	
AEGL-1 (Nondisabling)	25 (17)	25 (17)	25 (17)	25 (17)	25 (17)	25 (17)	No-observed-adverse-effect-level (NOAEL) for irritation (MacEwen et al., 1970); Verberk, 1977
AEGL-2 (Disabling)	380 (266)	270 (189)	160 (112)	110 (77)	110 (77)	110 (77)	Irritation: Eyes and throat; urge to cough (Verberk, 1977)