

*Archives of Industrial Health*. 12:623–627.

h. Nelson, K.W.; J.F. Ege, Jr.; M. Ross; L.E. Woodman; and L. Silverman. 1943. Sensory response to certain industrial solvent vapors. *Journal of Industrial Hygiene and Toxicology*. 25:282–285.

8. *Phosphorus oxychloride*—i.

*Description*. Phosphorus oxychloride (CAS No. 10025–87–3), a colorless fuming liquid with a pungent odor, is stable to above 300° C but is highly reactive with water yielding phosphoric acid and hydrogen chloride. It is used in the manufacture of plasticizers, hydraulic fluids, gasoline additives, fire retarding agents, and in the manufacture of alkyl and aryl orthophosphate triesters.

Information regarding exposure of humans to phosphorus oxychloride are limited to qualitative reports that indicate notable dermal, ocular, pharyngeal and pulmonary irritation following acute and subchronic (intermittent) exposures. Most reports lacked exposure terms although one report of occupational exposures indicated that air concentrations of phosphorus oxychloride ranged from 1.6 to 11.2 ppm. The effects often persisted after cessation of exposure, especially in those individuals experiencing more severe effects. Neither odor detection data nor lethality data are available for humans.

Quantitative data in animals are limited to reports of lethality. These data include a 4-hour LC<sub>50</sub> for rats (44.4 ppm) and guinea pigs (52.5 ppm), and an unverified 4-hour LC<sub>50</sub> of 32 ppm for rats. A 5–15 minute exposure of rats and guinea pigs to 0.96 ppm phosphorus oxychloride was noted as a “threshold

response” in a Russian report. A brief report from industry indicated immediate adverse responses (at 2 minutes) and death (18 minutes) following exposure to a very high concentration (25,462 ppm). The available studies affirm the extreme irritation properties of phosphorus oxychloride, although the exposures described also resulted in lethality. No information was available regarding reproductive/developmental toxicity, genotoxicity, or carcinogenicity.

There are no definitive data regarding the metabolism or precise mechanism of action of phosphorus oxychloride toxicity. Based upon the limited human and animal toxicity data, and the chemical properties of phosphorus oxychloride, it may be assumed that the primary effect involves damage to epithelial tissue and, for respiratory effects, subsequent pulmonary edema. The lethal potency of phosphorus oxychloride, however, does not appear to be explained simply by the activity of its degradation products (phosphoric acid and hydrogen chloride).

In the absence of odor detection data and quantitative data pertaining to effects consistent with AEGL-1 definition, AEGL-1 values were not developed.

Exposure-response data pertaining to AEGL-2 level effects were unavailable and, therefore no AEGL-2 values were developed. Because of the lack of exposure-response data for any effects, estimating AEGL-2 values by a reduction in AEGL-3 values was considered tenuous and difficult to justify.

AEGL-3 values were developed using an estimate of the lethality threshold

based upon the 4-hour LC<sub>50</sub> of 48.4 ppm in rats that was reported by Weeks et al. (1964). Although exposure-response data were unavailable, the lethality threshold was estimated a one third of the 4-hour LC<sub>50</sub> (i.e., 48.4 ppm/3 = 16.1 ppm). Due to uncertainties regarding species variability in the lethal response to phosphorus oxychloride and the lack of lethality data in humans, an order-of-magnitude uncertainty adjustment was applied for interspecies variability. Contact irritation resulting in damage to epithelial tissue appears to be involved in the toxic response to phosphorus oxychloride. It is likely that this response is a function of the extreme reactivity of phosphorus oxychloride with tissues (e.g., pulmonary epithelium) and not likely to vary greatly among individuals. The uncertainty adjustment for intraspecies variability, therefore, was limited to 3. The concentration exposure time relationship for many irritant and systemically acting vapors and gases may be described by  $C^n \times t = k$ , where the exponent, n, ranges from 0.8 to 3.5. In the absence of an empirically derived exponent (n), and to obtain conservative and protective AEGL values, temporal scaling was performed using n = 3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points using the  $C^n \times t = k$  equation.

The range of interspecies variability remains uncertain due to limited animal data and the absence of quantitative exposure-response data for humans. The absence of exposure-response data for non-lethal effects in animals or humans is a significant data deficiency.

The proposed AEGL values are listed in Table 9 of this unit.

TABLE 9.—SUMMARY OF PROPOSED AEGL VALUES FOR PHOSPHORUS OXYCHLORIDE

Classification	10-minutes	30-minutes	1-hour	4-hours	8-hours	Endpoint (Reference)
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR	Data unavailable for development
AEGL-2 (Disabling)	NR	NR	NR	NR	NR	Data unavailable for development
AEGL-3 (Lethal)	1.1 ppm (6.9 mg/m <sup>3</sup> )	1.1 ppm (6.9 mg/m <sup>3</sup> )	0.85 ppm (5.3 mg/m <sup>3</sup> )	0.54 ppm (3.4 mg/m <sup>3</sup> )	0.27 ppm (1.7 mg/m <sup>3</sup> )	Weeks et al., (1964). Estimate of lethality threshold in rats (16.1 ppm) based upon 3-fold reduction in 4-hour LC <sub>50</sub> of 48.4 ppm.

NR: Not recommended. Numeric values for AEGL-1 and AEGL-2 are not recommended due to the lack of available data. Absence of AEGL-1 and AEGL-2 values does not imply that exposure below the AEGL-3 is without effect.

ii. *References*. Weeks, M.H.; Mussleman, N.P.; Yevich, P.P.; Jacobson, K.H.; and Oberst, F.W. 1964. Acute vapor toxicity of phosphorus oxychloride, phosphorus trichloride and

methyl phosphonic dichloride. *Industrial Hygiene Journal*. 25:470–475.

9. *Phosphorus trichloride*—i.

*Description*. Phosphorus trichloride (CAS No. 007719–12–2) is a colorless, clear fuming liquid with a pungent,

irritating odor. In the presence of water, the chemical decomposes rapidly in a highly exothermic reaction to phosphonic acid, hydrogen chloride, and pyrophosphonic acids.