# MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

## INTEROFFICE COMMUNICATION

October 4, 2000

TO: File for polypropylene glycol (mole. wt. 999) (25322-69-4)

FROM: Marco Bianchi, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for polypropylene glycol (MW 999), is 49 $\mu g/m^3$ based on an annual averaging time. Hereafter, polypropylene glycol will be referred to as "P" followed by the average molecular weight.

The following references or databases were searched to identify data to determine the ITSL: IRIS-online, HEAST, NTP Management Status Report-online, RTECS, EPB-CCD, EPB library, CAS-online, NLM-online, IARC-online, NIOSH Pocket Guide, ACGIH Guide, ATSDR-online, and Patty's Industrial Hygiene and Toxicology.

After reviewing the above databases for data on polypropylene glycol, Patty's Industrial Hygiene and Toxicology was used as the main source of information for this chemical evaluation. An attempt was made to obtain copies of the original studies, but this effort proved unsuccessful. The Dow Chemical Company sent a *Workplace Environmental Exposure Level Guide* for polypropylene glycols published by the American Industrial Hygiene Association, but this document was fully summarized in Patty's Industrial Hygiene and Toxicology.

The polypropylene glycols are clear, lightly colored, slightly oily, viscous liquids that have very low vapor pressures. All of these materials are quite stable chemically and do not present hazards of flammability except at elevated temperatures. This family of compounds has a variety of uses, such as lubricants, solvents, plasitizers, antifoaming agents, etc.

Industrial exposure is most likely to be by direct contact with the skin and eyes. The very low volatility of these materials makes inhalation improbable except perhaps where mists are formed from violent agitation or high temperatures. The low-molecular-weight P(200-1200) have an appreciable acute oral toxicity causing central nervous system stimulation. They are also mildly irritating to the eyes, but are not irritating to the skin. Although these compounds can be absorbed through the skin to some extent, skin penetration does not seem to present a serious industrial hazard.

Acute oral rat toxicity studies have shown that low-molecular-weight P (400-1200) are rapidly absorbed. Excitement and convulsions appear in test animals within minutes after administration. With the higher-molecular-weight P (>2000), no excitement or convulsions were observed. Necropsy of animals one to eight days after exposure to the highest doses revealed nothing remarkable. In an acute inhalation study, five male rats were exposed for 7 hours to saturated concentrations of P1200. Two of these test animals were exposed to vapors generated at 100°C. There were no clinical signs of toxicity in rats exposed to vapor generated at room temperature, but the two animals exposed to vapors generated at 100°C had lungs rales or a bloody discharge (Cosmetic Ingredient Review, 1994).

In a subacute oral toxicity study, P1200 was fed to dogs and rats in their diets for 90 days at concentrations of 0.0, 0.1, 0.3, and 1 percent. Groups of two dogs of each sex received dietary levels of polypropylene glycol and a group of three of each sex served as the control group. Groups of 25 rats of each sex constituted all four of the groups. Male dogs on the 1% diet received from 317 to 380 mg/kg of the P1200 whereas the females received from 275 to 501 mg/kg. The average daily dose for the male rats on the 1% diet was 526 mg/kg and for the female rats, 810 mg/kg. On the 0.3% diet, the male dogs received daily doses averaging from 77 to 99 mg/kg; the female dogs, 90 to 123 mg/kg; the male rats, 157 mg/kg; and the female rats, 189 mg/kg. This study showed no evidence of adverse histopathological, hematologic, or clinical chemical or other effects from consumption of the chemical with the exception of body weight gains in dogs and rats at the high level (1%). On completion of the experiment, the high-level group of dogs showed net losses in body weight. The high-level rats, compared with the nonmedicated controls, showed less gain in body weight.
The 0.3% dietary concentration appears to be the no-observable-adverse-effect-level (NOAEL).

Other subacute toxicity studies using similar molecular weight polypropylene glycols have shown comparable results to compound related effects at the 1% dietary level. Small groups of male rats were maintained for 100 days on diets containing 0.1 and 1% of P750 and 0.1, 0.3, 1 and 3% of P2000. Those animals that received the diet containing 0.1% of P750 were unaffected as judged by studies of mortality, growth, organ weights, and gross and microscopic examination of the principal internal organs. The animals that received the diet containing 1% of P750, were judged by the same criteria, exhibited only a slight increase in the weight of the livers and kidneys without histological changes. Hematologic studies on this latter group of animals failed to reveal any abnormalities. One percent of P750 in the diet was well accepted by the rats, and there was no evidence of any of the pharmacological signs (excitement, tremors, convulsions) seen in the acutely poisoned animals. It is postulated that the material is readily metabolized or eliminated when absorbed in small doses, accounting for the apparent lack of physiologic effects. The rats that received 0.1, 0.3, and 1% of P2000 suffered no ill effects as judged by the criteria listed above. Hematologic studies were conducted only at the 1% level, with all values falling in the normal range. Although the growth of those animals maintained on the diet containing 3% of the P2000 was slightly below normal during most of the test period, there were no other changes attributable to the experimental diets.

Of the three subchronic oral studies presented above, the P2000 study was considered inappropriate for an ITSL derivation. Polypropylene glycols having molecular weights of >2000 do not have the same toxicologic effects of the lower molecular weight compounds, such as P750 or P1200. Since the toxicity of polypropylene glycol is dependent on the molecular weight of the compound, P750 and P1200 are close enough in molecular weight to P999 and equally bound this compound to sufficiently characterize its toxicity. Although both of these studies provide enough information to derive an ITSL, the P1200 study seems more appropriate to use.

In the P1200 study, two test species were used resulting in similar toxicologic endpoints. Default animal biologic values weren't necessary because actual body weights and ingestion rates from test animals were used to convert dietary dose levels into doses per body weight (mg/kg). Additionally, the rat P1200 study used more dose groups than the other subchronic oral studies which better characterized the toxicity of P1200. Therefore, a NOAEL of 0.3% (157 mg/kg) established for male rats from the P1200 study will be used to derive an ITSL for polypropylene glycol.

The ITSL will be calculated using methods described under R232 (1)(e); procedures for 7-day oral toxicity studies. The uncertainty factor of 35 which is typically reduced to 10 when a toxicity study is 90-days or longer will be kept at 35 due to the following uncertainties. First, a copy of the full study could not be obtained preventing independent critical interpretation of the test data. Secondly, the P1200 study can only approximate the toxicity of P999. Only by conducting a toxicity study for P999 can the true toxicity be known.

*The ITSL was derived as follows:*

NOAEL = 157 mg/kg
$W_A$ = body weight of experimental animal in kilograms (kg)
$I_A$ = daily inhalation rate of experimental animal in cubic meters/day ($m^3$)
b = absroption efficiency by the oral route of exposure
a = absroption efficiency by the inhalation route of exposure
35 = uncertainty factor; to account for using a NOAEL for a 7-day exposure period to estimate a NOAEL for a lifetime study.
100 = uncertainty factor; to account for specie differences and human population sensitivities.

$$ITSL = \frac{NOAEL}{35 \times 100} \times \frac{W_A}{I_A} \times \frac{b}{a}$$

$$ITSL = \frac{157 mg/kg}{35 \times 100} \times \frac{1}{0.916\ m^3/kg} \times \frac{1}{1}$$

$$ITSL = 0.049\ mg/m^3$$

***Conversion of $mg/m^3$ to $ug/m^3$***

$$ITSL = 0.049\ mg/m^3 \times \frac{1000\ \mu g}{1\ mg} = 49\ \mu g/m^3$$

**The ITSL for polypropylene glycol = 49 $\mu g/m^3$ based an annual averaging.**

**References:**


1. Clayton & Clayton eds. 1994. . Glycols [polypropylene glycols]. Patty's Industrial Hygiene and Toxicology. 4th ed. Volume II, Part F. pp. 4683-4687.

2. Cosmetic Ingredient Review Expert Panel. 1994. Final report on the safety assessment of propylene glycol and polypropylene glycols. Journal of the American College of Toxicology. 13(6):437-491.


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