method of Thompson [7] was used for the calculation of either the range finding or the advanced L.D.$_{50}$, both of which are based on 14-day periods of observation of the dosed animals. For the determination of the range finding L.D.$_{50}$ (R.F. L.D.$_{50}$) five animals were used on each of three or four dose levels differing by a factor of 2. Similarly, 10 animals were used on each of four dose levels differing by a factor of 1.26 for the determination of the advanced L.D.$_{50}$ (Adv. L.D.$_{50}$). In certain instances it was impossible to calculate the fiducial range, namely: when all rats survived at one dose level and all died at the next higher level. The intravenous R.F. L.D.$_{50}$ for polypropylene glycol 1025 was calculated on actual mortalities of five of five rats at 0.252 ml./Kg., three of five at 0.126 ml./Kg. and predicted mortalities of none of five rats for doses of 0.063 and 0.031 ml./Kg. The latter two levels were not given because of the technical difficulties involved in injecting amounts smaller than 0.01 ml. into the tail vein of rats.

A summary of the findings on current production lots of these glycols is presented in the table. The L.D.$_{50}$ data are set forth in terms of both grams and millimoles of compound per kilogram of body weight. The L.D.$_{50}$ in Gm./Kg. may be considered as indicating the practical hazard of a compound whereas the L.D.$_{50}$ in mμ/Kg. better expresses the actual quantitative toxicity. It is apparent from inspection of the table that by either method of evaluation

The Acute Toxicity (L.D.$_{50}$) of the Polypropylene Glycols Administered to Rats by Various Routes

Compound	Route: Oral* Gm./Kg.	Oral* Mμ./Kg.	Intraperitoneal Gm./Kg.	Intraperitoneal Mμ./Kg.	Intravenous Gm./Kg.	Intravenous Mμ./Kg.
Dipropylene glycol	14.85 (10.65-20.72)	110.68	10.59 (5.94-17.93)	78.93	5.80 (N. R. C.)†	43.23
Polypropylene glycol 425	2.91 (2.65-3.19)	6.85	0.46 (0.30-0.70)	1.08	0.41 (0.31-0.54)	0.96
Polypropylene glycol 1025	2.15 (1.19-2.41)	2.10	0.23 (0.15-0.36)	0.22	0.12 (0.084-0.16)	0.12
Polypropylene glycol 2025	9.76 (8.85-10.76)	4.82	4.47 (2.79-7.15)	2.21	0.71 (N. R. C.)	0.35

* For oral doses the material was used as a 20 per cent solution or suspension in water. In all other cases it was used undiluted. The numbers in parentheses indicate the fiducial range ($p = 0.05$) of the L.D.$_{50}$ expressed as grams per kilogram.
† No range was calculable. See text for explanation.

dipropylene glycol is less toxic for rats by any of the three portals of entry than the polypropylene glycol series. Furthermore, the molar toxicity of the latter compounds reaches a peak at a molecular weight of 1025 and then declines.

Oral doses of these compounds, within the ranges given for the L.D.$_{50}$ values, caused sluggishness, prostration, tremors, convulsions, and rapid death. Gross pathologic changes observed in rats which died included minor hemorrhage of the lungs, congestion of the liver and the spleen, ischemia of the kidney, and injection of the blood vessels of the intestines.

Lethal intraperitoneal doses of dipropylene glycol caused narcosis, while tremors, prostration, frothing at the mouth, and audible rales preceded death from doses of polypropylene glycols 425, 1025 and 2025.

The symptoms prior to death following intravenous injection were quite similar to those following intraperitoneal administration except that polypropylene glycols 1025 and 2025 caused convulsions. It is of interest that polypropylene glycol 425 proved to be twice as toxic to rats when injected as a 20 per cent aqueous solution than when given undiluted. This observation was made on two different samples of polypropylene glycol 425 and is contrary to the general observation that a compound diluted with water is no more toxic than the undiluted substance.

Evaluations of skin penetration according to the method of Draize [8] demonstrated that polypropylene glycols 1025 and 2025 do not penetrate the skin readily as groups of five rabbits on a

7. Thompson, W. R.: Use of Moving Averages and Interpolation to Estimate Median-effective Dose, Bact. Rev. **11**:115-145, 1947.

8. Draize, J. H.: Woodard, G., and Calvery, H. O.: Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes, J. Pharmacol. & Exper. Therap. **82**:377-390, 1944.