I. Effect of SKF-525-A (β-diethylaminethyldiphenylpropyl-acetate) and AT (3-amino-1,2,4-triazole) on the Metabolism of Inhaled Vinyl Chloride Monomer (VCM) in Rats:

Further experiments have been completed to verify the effect of SKF-525-A on the metabolism of inhaled VCM in rats. The inhalation apparatus and methods described in our earlier paper, "Preliminary Studies of the Fate of Inhaled Vinyl Chloride Monomer (VCM) in Rats", were used in these experiments. Table 1 illustrates the experimental results. SKF-525-A pretreatment clearly inhibits VCM metabolism at VCM exposure concentrations of approximately 1000 ppm, but has little effect on the metabolism of VCM at exposure concentrations below 100 ppm.

1000 mg/kg AT has been shown to inhibit 90% of the liver catalase activity of rats following a 3 hour pretreatment. (Heim, Appleman and Pyfrom, 1955). Therefore, if an oxidation of 2-chloroethanol a postulated VCM intermediary metabolite occurred, via hydrogen peroxide and catalase, AT pretreatment should have an inhibitory effect. Pretreatment of rats with 1000 mg/kg AT 256 minutes prior to exposure to approximately 1000 ppm VCM for 60 minutes induced a 16.37% depression of VCM metabolism.

In a single preliminary experiment, a 180 minute pretreatment with 1000 mg/kg AT and a 50 minute pretreatment

with 75 mg/kg SKF-525-A, followed by exposure to approximately 1000 ppm VCM for 82.5 minutes, induced 20.69% depression of VCM metabolism. This degree of depression is somewhat greater than that induced by SKF-525-A or AT alone, and may indicate an additive effect of the two inhibitors. Thus one might conclude that oxidative pathways involving the peroxide of 2-chloroethanol and the epoxide of VCM may both operate simultaneously, when the metabolism of VCM via alcohol dehydrogenase is saturated by exposure to 1000 ppm VCM.