

Vinyl chloride
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STATEMENT ON VINYL CHLORIDE RESEARCH

It is well known that toxic effects are caused by absorption into the body of excessive amounts of any substance. When this occurs the capacity of the body's normal defense mechanisms are exceeded and this may result in more or less serious consequences - as with an excessive intake of alcohol. However, when the amount absorbed does not exceed this capacity the body is capable of dealing with it without toxic effects.

Research on vinyl chloride (VC) in rats has demonstrated that high doses of VC are handled in the body differently than low doses. The results indicate that low doses of VC are readily detoxified, but high doses of VC exceed the body's normal defense mechanisms and detoxification is slowed and perhaps changed. Therefore, exposure to high levels of VC in rats results in an increased susceptibility to toxic effects including cancer. From data available, it appears that induction of cancer is correlated with high doses of VC where detoxification is slowed, altered or incomplete, and that cancer is not induced at low doses where the body's normal defense mechanisms remain fully operative.

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Summary of the Studies on the Pharmacokinetics of
Vinyl Chloride in Rats and its Possible Relationship
to Oncogenicity

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ABSTRACT

Studies on the fate of ^{14}C -labeled vinyl chloride (VC) following oral administration and inhalation exposure in rats demonstrated that the disposition of VC in the body is a function of the dose. As the dose or exposure level of VC is increased the metabolism or detoxification pathways become saturated. VC is detoxified primarily by conjugation with nonprotein sulfhydryl groups in the liver (primarily glutathione, GSH). Studies to characterize the depression of liver GSH as a function of magnitude and duration of exposure to VC have shown that a single 7 hour exposure of rats to 100 ppm or greater results in an unequivocal depression of liver GSH. Exposure to 10 ppm VC for 7 hours did not result in any depression of liver GSH. These results suggest that increasing doses of VC deplete liver GSH and consequently lower the body's defense mechanism for detoxification of the reactive metabolites of VC. This increased susceptibility may

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result in induction of carcinogenesis, and from data available, it appears that a correlation exists between doses of VC which cause tumors and those that saturate metabolic or detoxifying pathways.

Conceptually, the results of these investigations indicate that statistical projections utilizing data collected from rats exposed to high doses of VC are invalid for predicting the hazard of low level exposure because such projections assume that the dynamics governing the fate of VC in the body are unaltered; and in fact, the data presented demonstrate that the fate of VC in rats is highly dependent on the dose administered.

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