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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM **6(A)(2) DATA**

Subject: **GLUTARALDEHYDE. ID# 043901**. Review of studies on compatibility of glutaraldehyde with blood and subchronic intravenous toxicity in rat.

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I. CONCLUSIONS

No imminent hazard was identified for glutaraldehyde in the submitted in vitro and in vivo studies (see summaries in Discussion section, below, for additional details). Glutaraldehyde at low concentrations did not cause hemolysis in human blood in vitro (4 ppm glutaraldehyde solution added to give unspecified final concentration in blood). Rats given single or repeated intravenous doses of glutaraldehyde up to 6 ppm (up to 1.5 μg glutaraldehyde/animal) showed no effects on mortality, body weight, selected hematology or clinical chemistry parameters or gross/microscopic pathology of selected major organs.

Although no overt toxicity was observed in these studies and the data suggest that intravenous exposure to small amounts of glutaraldehyde do not cause hemolysis or significant adverse effects, the data are not conclusive since (1) a limited number of toxicity

endpoints were evaluated; (2) the relationship of the concentrations tested in these studies to potential concentrations from accidental exposures during hemodialysis was not indicated and (3) the studies did not test at higher concentrations of glutaraldehyde to establish intravenous doses at which effects from intravenous exposure would be observed.

II. ACTION REQUESTED

Union Carbide Corporation (in a letter from Joan Young dated 3-29-96) submitted summaries of the following studies on the effects of glutaraldehyde on blood: an in vitro direct contact hemolysis test using human blood, an in vivo blood compatibility study in the rat (both MRID 43973301) and a subchronic intravenous toxicity study in the rat (MRID 43973302). These data were submitted as information pertaining to the potential for toxicity to humans via intravenous exposure in clinical situations, for example from accidental exposure during hemodialysis if glutaraldehyde used to sterilize re-use dialysis equipment was not rinsed out completely. This package was submitted as 6(A)(2) data.

III. DISCUSSION

The following summaries briefly describe each study and are based on summaries of the studies prepared by Dr. Brian Ballantyne. Detailed study reports were not submitted. [One-liners for these studies were not prepared because of the lack of detail in the study reports and the limited information they provide.]

COMPATIBILITY OF GLUTARALDEHYDE WITH BLOOD (FDRL REPORT NO. 7400, OCTOBER 22, 1982; MRID 43973301)

1. *IN VITRO* DIRECT CONTACT HEMOLYSIS TEST (HUMAN BLOOD)

"Activated" glutaraldehyde solutions (activator not specified) at 2 and 4 ppm in normal saline were added to samples of human blood that were anticoagulated using EDTA (volume ratio of glutaraldehyde solution to blood not indicated). Following a 1-hr incubation at 37°C, samples were centrifuged at 2500 rpm for 10 min and the supernatant plasma was read spectrophotometrically at 545 nm using a distilled water blank.

The mean % hemolysis observed was 0.26% and 0.3% in blood samples to which 2 ppm or 4 ppm glutaraldehyde had been added, respectively. These results indicated the absence of significant hemolysis. However, it could not be determined from the submitted summary what the final concentration of glutaraldehyde was in the blood samples, or how it might relate to potential exposure levels.

2. *IN VIVO* COMPATIBILITY STUDY IN THE RAT

Six male Sprague Dawley rats/group were given intravenous injections of 0.3 ml distilled water or 0.3 ml of 2 ppm or 4 ppm glutaraldehyde solution in the jugular vein.

Blood was collected after 4 hr from the orbital venous plexus and evaluated for selected hematology parameters (hemoglobin concentration, hematocrit, prothrombin time) and clinical chemistry parameters (BUN, total protein, creatinine, uric acid, Na+, K+, Mg+, Cl-, phosphorus and SGOT/SGPT. In addition, animals were observed for clinical signs of toxicity for 4 hr post-dosing and examined for gross pathology after 4 hr.

There were no effects on any parameter evaluated in this study.

SUBCHRONIC INTRAVENOUS TOXICITY STUDY IN THE RAT (TOXIGENICS REPORT 410-1088, APRIL 6, 1983; MRID 43973302)

Fifteen male CD albino rats/group were given intravenous injections of distilled water or "activated" glutaraldehyde solutions (activator not specified) at concentrations of 3 or 6 ppm, 3 times per week over a period of 90 days (total of 39 injections). Dose volume was 1 ml/kg body weight in all groups. [Note: in comments on this study Dr Ballantyne estimated that the dose to each animal was approximately 0.75 μg (3 ppm) or 1.5 μg (6 ppm) glutaraldehyde.] Animals were evaluated daily for clinical signs of toxicity and weekly for body weight gain. Blood was collected from 10 animals/group on the day of sacrifice for evaluation of hematology (hemoglobin concentration, erythrocyte count, hematocrit, leucocyte count and platelet count) and for clinical chemistry parameters (SGOT/SGPT and alkaline phosphatase).

No effects on any parameter evaluated were observed.