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Document Title

BUTYL CELLOSOLVE FOUR HOUR LC50 INHALATION STUDY ON RATS AND ACUTE TOXICITY AND PRIMATY IRRITANCY STUDIES ON UCAR AW-100 AND UCAR AW-200 WITH COVER LETTER DATED 102088

Chemical Category

BUTYL CELLOSOLVE

UNION CARBIDE

UNION CARBIDE CORPORATION
Health, Safety and Environmental Affairs
Chemicals and Plastics Group

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Document Control Officer
(Atten: Section 8(e) Coordinator)
Information Management Division
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

Dear Sir or Madam:

Union Carbide (UCC) is by this letter submitting results of three studies pertaining to 2-butoxyethanol (CAS No. 111-76-2). UCC believes that the studies contain information which may be of interest to the EPA, and has decided to submit them as For Your Information (FYI).

In the test results, discoloration, necrosis, and subsequent loss of the distal portion of the tail were observed in rats following exposure to 2-butoxyethanol via either (1) single 4-hour inhalation exposure to potentially lethal concentrations or (2) oral administration of high doses. This submission relates to findings of acute tests reported by the Bushy Run Research Center.

UCC does not believe that these results reasonably support a conclusion of substantial risk of injury to human health. However, these findings are being submitted because the Agency has indicated an interest in this type of phenomenon in 8EHQ-1279-0325, which pertained to similar observations regarding the tails of rats following dietary administration of trithiocyanuric acid.

The findings related to tail necrosis and/or loss, as well as other major signs of toxicity following exposure to 2-butoxyethanol, are summarized as follows:

A. 2-Butoxyethanol; Four-Hour LC50 Inhalation Study on Rats Bushy Run Research Center Project

Six rats/sex/group were exposed by inhalation to 202, 523 or 867 ppm of 2-butoxyethanol vapor for a single 4-hour exposure. Observations on animals

in the 867 and 523 ppm groups were death, loss of coordination and reddish fluid on the skin and hair of the urogenital region; 2 of 4 male and 2 of 3 female survivors in the 523 ppm group had dry gangrenous tails. Necropsy of the animals that died revealed enlarged and discolored kidneys, and the bladder contained red-stained urine. The only related observation in the 202 ppm group was the presence of a slight amount of dried red material on the tails of male and female rats. LC50 values were found to be 486 ppm and 450 ppm for males and females, respectively.

B. UCAR AW-100 and UCAR-200; Acute Oral Toxicity in Rats Bushy Run Research Center Project Report

UCAR AW-100 and UCAR-200 contain 21.1% and 38.8% 2-butoxyethanol, respectively. AW-100 and AW-200 are water-borne dispersions of a vinyl interpolymer containing hydroxyl and carboxyl groups (generic name), the other components of which (excluding minor impurities) are 2-butoxyethanol and water. Signs of toxicity following single peroral administration to the rat included darkening of the tail areas with subsequent tail loss as well as sluggishness, labored breathing, piloerection and lacrimation. Necropsy findings included red-black fluid in the bladder, red-black cortical and medullary regions in the kidney and necrosed tails. LD50 values for UCAR AW-100 and UCAR AW-200 were 11.3 and 5.84 m./kg, respectively, in males and 4.29 and 2.54 ml/kg in females. For both test materials, tail effects were seen at dose levels of 2 ml/kg (lowest dose administered) and above.

To investigate whether the constituent 2-butoxyethanol might be responsible for producing the effects of UCAR AW-100 and UCAR AW-200 on rat kidneys and tails, 3 rats/sex/dose group were dosed orally with a 17% dilution of 2-butoxyethanol in distilled water at 4.0 and 8.0 ml/kg of dilution. Results with the 2-butoxyethanol dilution were similar to those seen with the 2 UCAR formulations. All males survived and all females died. Many signs of toxicity were recorded, including darkening and partial loss of the tails and red urine. Postmortem examination revealed areas of necrosis on the tails, red-black fluid in the urinary bladders and kidneys and red-black cortical and medullary regions. Sections of tissue from the tail and kidneys of several animals treated with the UCAR formulations or 2-butoxyethanol in distilled water were examined microscopically. Detailed results are included in study reports. All of the animals examined, whether treated with either of the 2 formulations or with the 2-butoxyethanol solution alone, had similar histologic processes. It was, therefore, concluded that the adverse effects observed with UCAR AW-100 and AW-200 were attributable to the 2-butoxyethanol component. The pathogenesis of the lesions in the tail was attributed to thrombosis of the larger arteries of the tail with secondary ischemia developing. The specific cause of the vascular thrombosis was not determined, but was most likely a secondary event associated with the well-established hemolytic activity of this chemical in the rat (i.e., crystallization of hemoglobin in the blood vessels). Human erthrocytes have been shown to be resistant to such hemolytic assault[2].

Except for the specific effect on the tails of the rats, as observed in the studies cited above, the toxicity of 2-butoxyethanol in rats and other laboratory animal species has been widely recognized and reported in the scientific literature for over forty years. A hemolytic effect in rats, a process which may be related to the apparent thrombosis, subsequent ischemia and eventual necrosis of the tail, was reported by Werner et al. (1943)[1] and

Carpenter et al. (1956)[2]. The latter also reported that humans were more resistant than rats or other laboratory animals to the hemolytic effects of 2-butoxyethanol. The significance of necrosis and partial loss of tails of rats exposed to high levels of 2-butoxyethanol has not been established with respect to potential correlative effects in humans. The studies performed at Bushy Run Research Center did not establish a mechanism of action for this effect, and therefore the nature of any proposed analogous effect in humans exclusive of the hemolytic process is even more remotely speculative, above and beyond the obvious lack of an anatomic correlate.

Information on 2-butoxyethanol has been previously reported to the Agency under Section 8(e). The submission, designated 8EHQ-0483-0475, included findings which were reported in a study of the inhalation teratogenic potential of 2-butoxyethanol in the rat, with daily exposure of dams to vapor concentrations of 0, 100, 200 or 300 ppm, 6 hours/day, on gestation days 6 through 15. It is interesting to note that, although exposures to the vapor "resulted in a dose-related increase in the frequency of signs indicative of hematuria" in the dams, effects on the tail were not noted in the status report for this submission. This would suggest that the tail effects occur at levels of exposure which exceed those required to elicit hemolysis, and adds further support to a theory that this phenomenon may in fact occur secondary to extensive hemolysis.

In the attached reports, the term "CONFIDENTIAL" is entered on the first page and elsewhere in the report. These are simply a precautionary statement for internal use at the time of issuance of the reports. You are advised, however, that the publication rights to the contained information are the property of Union Carbide Corporation.

If there are any questions concerning these submissions, please contact Dr. W. C. Kuryla (203) 794-5230 or my staff.

Very truly yours,

R E Bollinger

R. E. Bollinger
Director, Occupational Health
and Product Safety/Liability

REB/pjm
Attachments

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1. Werner, H.W., Nawrocki, C.Z., Mitchell, J.L., Miller, J.W. and von Oettingen, W.F. (1943). "Effects of repeated exposures of rats to vapor of monoalkyl ethylene glycol ethers." J. Ind. Hyg. Toxicol., 25, 374-379.

2. Carpenter, C.P., Possani, U.C., Weil, C.S., Nair (III), J.H., Keck, G.A. and Smyth (Jr.), H.F. (1956). "The Toxicity of Butyl Cellosolve Solvent," Arch. Ind. Health, 14, 114-131.