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UNION CARBIDE CORPORATION 39 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001

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March 16, 1994
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Office of Pollution Prevention & Toxics
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460



8EHQ-94-12950
INIT 03/22/94

OFFICE OF POLLUTION PREVENTION & TOXICS

Attn: 8(e) Coordinator



88940000192

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") herewith submits the following information arising from unusual observations during acute toxicity testing of isobutanol (CASRN 78-83-1). It is not possible at this point to judge whether the observations bear any relevance to human health hazard evaluation. However, the information is being submitted to assure satisfaction of any reporting obligation which EPA may deem to exist under TSCA Section 8(e).

In studies designed to assess the acute toxicity of isobutyl alcohol, two rats were observed, at necropsy, with deciduomas. One of the rats was in a group used to assess the acute oral toxicity and had received a dose of ~2.8 g/kg body weight, the other was in a group exposed to substantially saturated vapor (~13,000 ppm) for a 6-hour period (static conditions). These two animals were from a group of 33 rats of the Sprague Dawley strain and obtained from Harlan Sprague Dawley Inc., Indianapolis, Indiana. Additional studies are currently in progress in an attempt to determine whether the pseudopregnancy observed in these two animals was a spurious occurrence or related to isobutyl alcohol treatment.

Preliminary verbal information has been received from these follow-up studies. In a probe study 5 female Sprague Dawley rats from Harlan Sprague Dawley Inc. were dosed by gavage with 2830 mg/kg isobutyl alcohol. The animals were 13 to 14 weeks of age when dosed and were sacrificed 5 days after dosing. One of these animals died. In the definitive study, 15 females (of the same strain, age and supplier), were given the same dose again by gavage. In addition six control animals were included in the design. Surviving animals were sacrificed 14 days after dosing. Of the 15 dosed animals, 6 died. None of the 13 surviving

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animals (4 from the probe study and 9 from the definitive study) were observed with deciduomas.

Blood samples were taken for hormonal analysis. In most of the treated animals there appeared to be an increase, above normal values, in progesterone concentration within 1 to 3 days after dosing (reaching concentrations >85 ng/ml in some of the animals). At the same time there appeared to be decreases in estradiol concentrations. The effect of isobutyl alcohol on the hormonal changes appeared to resolve within ≈10 days after dosing. One of the six control animals demonstrated a similar trend. These changes are indicative of an interruption in the normal estrous cycle.

Union Carbide plans to attempt a rational evaluation of the data after the follow-up studies are completed and reported. We will provide a copy of the report and our evaluation to EPA at that time. For the present, we consider that there is no basis for any increased concern over potential exposure to isobutanol under regular and foreseeable conditions of handling and use.

Please contact the undersigned with questions, if any, at 203/794-5230.

Very truly yours,



William C. Kuryla, Ph.D.
Associate Director
Product Safety

WCK/jfh

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