

Procter & Gamble

The Procter & Gamble Company
Ivorydale Technical Center
5299 Spring Grove Avenue, Cincinnati, Ohio 45217-1087

(B)

November 22, 1995

ORIGINAL

Document Processing Center (TS-790)
(Attention: Section 8(e) Coordinator)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, S. W.
Washington, D. C. 20460

8EHQ-1195-13392

NO CBI

RECEIVED
NOV 24 AM 8:56

RE: TSCA Section 8(e) Submission for 2-Methyl-2,4-Pentanediol (CAS# 107-41-5)

ATTN: TSCA Section 8(e) Coordinator

This submission is made in accordance with TSCA Section 8(e) requirements and discharges any TSCA Section 8(e) responsibilities that exist for our Company regarding the information described herein. We do not believe the data described in this submission reasonably support the conclusion that the subject material presents a substantial risk of injury to human health or the environment.

Procter and Gamble on March 27, 1995 submitted to EPA under TSCA Section 8e the results of a range-finding Developmental Toxicity study with 2-Methyl-2,4-Pentanediol (CAS# 107-41-5). A definitive Developmental Toxicity study was initiated and completed with this substance.

This submission provides a draft summary of results for the definitive Developmental Toxicity Study in Rats with 2-Methyl-2,4-Pentanediol (CAS# 107-41-5) as test substance D1748.01. Developmental toxicity was evidenced by reduced mean fetal body weights and reduced gravid uterine weights at 1200 and 1600 mg/kg/day. One whole litter resorption occurred at the 1600 mg/kg/day dosage level. There was no statistically significant increase in malformations. Maternal toxicity was observed at the 1200 and 1600 mg/kg/day dosage levels evaluated. Also, ataxia was noted at 1200 mg/kg/day and above.

We have handled and will continue to handle this material with appropriate caution in keeping with our standard practice for handling all chemical substances. If you wish further information, please contact me.



8EHQ-95-13392
SP001 11/24/95

Very truly yours,

THE PROCTER AND GAMBLE COMPANY

W. E. Bishop, Ph. D.
Manager Risk, Policy & Regulatory Sciences
Telephone: 513/627-6145

RECEIVED
NOV 31 AM 8:12



89960000011

mm
3/11/96



2. SYNOPSIS

Mated Charles River Crl:CD® VAF/Plus® female rats, consecutively assigned to one control and three treatment groups of 30 animals each were used to determine the developmental toxicity, including the teratogenic potential, of the test article D1748.01 in pregnant rats. Dosage levels of 500, 1,200 and 1,600 mg/kg/day were administered by gavage as a single daily dose on gestation days 6 through 17 at a volume of 10.0 mL/kg. The control group received the vehicle only, distilled water, on a comparable regimen. Cesarean section examinations were performed on all remaining females on gestation day 20. A teratologic examination of the fetuses was then conducted.

Administration of D1748.01 to pregnant female Crl:CD® VAF/Plus® rats resulted in no deaths. One female from the 500 mg/kg/day group was necropsied on gestation day 20 following an early delivery. Maternal toxicity was indicated by an increased incidence of clinical observations including soft stool and decreased defecation at doses of 500 mg/kg/day and above and ataxia at 1,200 mg/kg/day and above. One female at the 1,600 mg/kg/day dosage level aborted prior to cesarean section and this finding was also considered indicative of maternal toxicity. Maternal toxicity was also indicated by a statistically significant reduction in mean weight gain at the 1,200 and 1,600 mg/kg/day dosage levels and mean weight loss at the 1,600 mg/kg/day level during intervals of the dosing period and throughout the study from gestation days 0-20 as compared with the control group. Maternal toxicity was also evidenced by a dose related reduction in mean carcass weight for all dose groups compared with the control group. Similarly, maternal toxicity was indicated by reduced food consumption at the 1,200 and 1,600 mg/kg/day dose levels during the dosing period and over the entire study for the 1,600 mg/kg/day group as compared with the 0 mg/kg/day group.

Developmental toxicity was evidenced by reduced mean fetal body weights and reduced gravid uterine weight at the 1,200 and 1,600 mg/kg/day dosage levels. Developmental toxicity was indicated at the 1,600 mg/kg/day dosage level by one abortion and one whole litter resorption. There was a non-statistically significant increase in the total number of malformations observed at the 1,200 (external only) and 1,600 mg/kg/day dosage levels compared with the control group. The incidence of fetal variations was increased at the 1,600 mg/kg/day dose level compared with the control group, however, the number of litters affected was comparable. The increased incidence of fetal malformations and variations at the 1,200 and 1,600 mg/kg/day dose levels was most likely the result of maternal toxicity characterized by reduced weight gain, reduced food consumption and increased clinical observations at the two highest dosages and was not considered a direct-acting teratogen.

DRAFT

0006



D to NOEL

The No Observable Adverse Effect Level (NOAEL) was not established with respect to maternal toxicity based on clinical observations, a reduction in body weight, carcass weight, and food consumption values at doses of 500 mg/kg/day and above. The NOAEL with respect to developmental toxicity was 500 mg/kg/day based on reduced fetal body weights and an increased incidence of malformations at the 1,200 and 1,600 mg/kg/day dosage levels compared with the control group. The developmental toxicity observed in this study was considered to be related to the toxicity experienced by the dams (maternal toxicity).

D to
NOEL

The maternal toxicity produced by the test article, D1748.01, was considered to have affected fetal body weights and gravid uterine weights and as a consequence the incidence of fetal malformations and variations was believed to be due to the toxicity experienced by the dam and not the result of a direct-acting teratogenic effect.