

Shell Oil Company



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



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Dear Sir:

SUBJECT: CENTRAL NERVOUS SYSTEM (CNS) DEPRESSION IN AN ACUTE
INHALATION NEUROTOXICITY STUDY OF ISOBUTANOL IN RATS

The following information is submitted under TSCA 8(e).

Following inhalation exposure of rats for 6 hours to vapor concentrations of 1500, 3000, and 6000 ppm isobutanol (CASN 78-83-1) in an acute neurotoxicity study, clinical signs of CNS depression at all doses and decreased motor activity at 6000 ppm were observed. Although isobutanol is known to be a CNS depressant at its 4-hour LC₅₀ vapor concentration of approximately 6300 ppm, the vapor concentrations reported in the present study are lower.

This study was sponsored by the Chemical Manufacturers Association Oxo Process Panel, to which Shell Oil Company is a member, as part of a program to evaluate the neurotoxicity potential of several industrial solvents. Attached is a copy of the summary of the unaudited progress report by Monsanto Environmental Health Laboratory, which was submitted to the CMA. The Agency will receive a complete final report from CMA when it is available.

This report is filed to provide information EPA may find useful. In no way is it intended as a waiver of any rights or privileges belonging to Shell Oil Company as the reporting corporation, its agents or employees. The reporting corporation, its agents and employees, reserve the right to object to this report's use or admissibility in any subsequent judicial or administrative proceeding against the corporation, its agents or employees.

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This report has been compiled based on information available as of the date of filing. The corporation, its agents and employees reserve the right to supplement the data contained in this report, and to revise and amend any conclusions drawn therefrom.

This report contains no confidential business information.

The following person should be contacted if you have questions or a need for discussion.

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Very truly yours,



R. N. Shulman, General Manager
Health, Safety, and Environment
Shell Oil Company

Attachment

THG/sjh

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SUMMARY

Four groups of 10 rats/sex were exposed by inhalation for 6 hours to vapors of isobutanol at 0, 1500, 3000, and 6000 ppm. Neurobehavioral tests (functional observational battery and motor activity) were conducted prior to exposure (pretest), immediately after exposure (day 0), the day after exposure (day 1), and 7 and 14 days after dosing. Each animal was sacrificed 15 days after exposure to isobutanol. Five animals from each group were perfused, and the female reproductive tract and selected central and peripheral nervous tissues from these animals were retained but were not microscopically examined. The remaining animals from each group were given a complete gross necropsy and their female reproductive tracts were retained.

Isobutanol clearly causes a rapidly reversible general depression of the central nervous system at concentrations of 3000 and 6000 ppm during a 6 hour exposure period. The transient decrease in alertness in female rats, transient decrease in motor activity in male and female rats, and transient, slight, incoordinated gait observed in one male rat are considered residual effects of the anesthetic effects of 6000 ppm level of isobutanol. There were no treatment-related effects in rats at the 3000 ppm level following acute exposure. Minimal effects (hypoactivity) were seen in rats at the 1500 ppm level during, but not after, the 6-hour exposure period. No treatment-related findings were observed in any tissues or organs during gross necropsy 15 days after exposures were conducted. The 1500 ppm level is considered to be a Lowest-Observable-Effect-Level (LOEL) for the study.

STUDY TITLE

Acute Neurotoxicity Study of Isobutanol in Sprague-Dawley Rats

DATA REQUIREMENT

40 CFR Part 799 Multi-Substance Rule for the Testing of Neurotoxicity
40 CFR Part 798.1150 Inhalation Test Guidelines

Test Guidelines 798.6050 & 798.6200 updated by
Neurotoxicity Guideline 81-8, Subdivision F

AUTHORS

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STUDY COMPLETED ON

PERFORMING LABORATORIES

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PROJECT NUMBER

Monsanto Laboratory Project Numbers: EHL 94009 (94010)
Union Carbide Laboratory Project Number: #37-AEG-131

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