

8EHQ-0497-13607



Shell Oil Company

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February 19, 1997



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U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460
ATTN: TSCA 8(e) Coordinator

Contains No CBI

Dear Sir:

SUBJECT: SUPPLEMENTAL TSCA 8(e) INFORMATION

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

A TSCA 8(e) on the subject of necrosis of olfactory epithelium in rat nasal passages following exposure to n-butyl acetate was filed on March 13, 1996 (copy attached) based on a technical review of a draft report of the study. The final report of that study is now available and is herewith provided to the EPA as a supplement to the original TSCA 8(e) information. This supplemental information is not believed to be significantly different from that reported previously.

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 Chemical 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.

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.



89970000127

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

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Manager, Product Safety and Compliance
Shell Chemical Company
P.O. Box 4320
Houston, TX 77210
Telephone No. 713-241-6958
Fax No. 713-241-3325

Very truly yours,

Attachment

THG/sjh

bc: without attachment
J. C. Willett
G. A. Van Gelder
T. H. Gardiner
M. I. Banton
J. S. Eastridge
C. F. Phillips
C. E. Ross
J. P. Sepesi
R. H. Dickehuth (SHR-328-96-01)

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March 13, 1996

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

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EPA/PT/STP

Dear Sir:

**SUBJECT: NECROSIS OF OLFATORY EPITHELIUM IN RAT NASAL PASSAGES
FOLLOWING EXPOSURE TO N-BUTYL ACETATE**

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

Following inhalation exposure of rats for 6 hours/day, 5 days/week, for 13 weeks to vapor concentrations of 0, 500, 1500, or 3000 ppm N-butyl acetate (CASN 123-86-4), necrosis of the olfactory epithelium of the nasal cavity was reported after exposure at the 1500 and 3000 ppm dose levels. No lesions were observed in the nasal passages of the 500 ppm group. The voluntary study was conducted by the Eastman Kodak Company Toxicological Sciences Laboratory for the Chemical Manufacturers Association Oxo Process Panel.

n-Butyl acetate is a solvent used in commercial products by Shell Chemical Company. Shell became aware of the information during technical review of the draft report of the study. A copy of the abstract to the draft report is attached. A copy of the final report will be provided when it is available.

Relevance of these findings to humans is unclear, since n-butyl acetate occurs naturally among numerous other propionates and butyrates in bananas and other fruit, and is used as a flavoring agent and solvent. It should also be noted that, since the study evaluated repeated daily exposures and demonstrated decreasing intensity of the effect with decreasing vapor concentration, it is unlikely that a single, brief exposure to low vapor concentrations of n-butyl acetate would produce adverse effects to the nasal cavity of humans. Moreover, the OSHA PEL TWA for n-butyl acetate is 150 ppm compared with a NOAEL for nasal effects in the 13-week study of 500 ppm.

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 Chemical Company as the reporting corporation, its agents or employees. The reporting corporation, its agents and employees,



Shell Chemical Company

Interoffice Memorandum

February 26, 1996

FROM: M.I. Banton

TO: T.H. Gardiner, ON-SITE-COORDINATOR

SUBJECT: SUSPECT HAZARD REPORT FOR n-BUTYL ACETATE

This memorandum is intended to provide documentation for the n-butyl acetate suspect hazard report.

Background. n-Butyl acetate was recently the subject of a 13-week subchronic inhalation toxicity study conducted by the Eastman Kodak Company Toxicological Sciences Laboratory. The purpose of this study was to evaluate the potential toxicity of this material to rats following 13-week repeated inhalation exposure. This study was conducted voluntarily by the Chemical Manufacturers Association Oxo Process Panel in parallel with a subchronic neurotoxicity study that was conducted under a consent agreement with the U.S. Environmental Protection Agency. The subchronic inhalation study is now complete and a draft report has been released to member companies for review.

Experimental Design. Male and female Sprague-Dawley rats were exposed to concentrations of 0, 500, 1500 or 3000 ppm of n-butyl acetate for 6 hours per day, 5 days per week for 13 consecutive weeks. During and/or after the exposure period, animals were evaluated for effects on mortality, body weight, feed consumption, ophthalmology, hematologic parameters, clinical chemistry parameters, organ weights, and gross and microscopic pathology.

Study Results. No spontaneous mortality occurred during the study. Animals exposed to 1500 and 3000 ppm n-butyl acetate displayed acute, transient signs of reduced activity levels during exposure. The 1500 ppm and 3000 ppm treatments also produced decreased body weight and feed consumption throughout much of the exposure period. The 500 ppm treatment resulted in reductions in feed consumption at a few time periods, however, this was not accompanied by a corresponding statistically significant reductions in body weight. No treatment-related ophthalmologic changes were observed in the treated animals. Effects on hematology, clinical chemistry and organ weights were unremarkable. Gross necropsy observations were limited to signs of irritation to the glandular stomach and necrosis in the non-glandular stomach in two 3000 ppm female rats. Microscopic examination of the tissues revealed exposure-related changes in the nasal passages and stomach of 1500 and 3000 ppm rats. All male and female 3000 ppm rats and 4/10 male and 6/10 female 1500 ppm rats had necrosis of the olfactory epithelium. The severity of the olfactory lesion was mild to moderate for the 3000 ppm group

and minimal to mild for the 1500 ppm group. No lesions were observed in the nasal passages of the 500 ppm group. A few (3/10) 3000 ppm female rats had inflammation of the stomach mucosa (glandular or forestomach). The severity was minimal to mild. No effects to the stomach mucosa were seen in the low- and mid-concentration groups.

Summary/Conclusion. Repeated exposure to 1500 and 3000 ppm n-butyl acetate vapor produced necrosis of the olfactory epithelium in rat nasal passages. To the best of my knowledge, this effect has not previously been reported for n-butyl acetate. A related ester, n-butyl propionate, has also produced olfactory epithelium necrosis following repeated inhalation exposure (SHR-324-95-06).

STUDY TITLE

n-BUTYL ACETATE

**A THIRTEEN-WEEK SUBCHRONIC INHALATION
TOXICITY STUDY IN THE RAT**

HAEL NO. 94-0305 KAN 900710
CAS NO. 000123-86-4

FINAL REPORT

AUTHORS

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PERFORMING LABORATORY

Toxicological Sciences Laboratory
Health and Environment Laboratories
Eastman Kodak Company
Rochester, New York 14652-6272
USA

LABORATORY PROJECT ID

940305I7

STUDY SPONSOR

Oxo Process Panel
Chemical Manufacturers Association
1300 Wilson Boulevard
Arlington, VA 22209

CMA REFERENCE NUMBER

OXO-17.0-BA-KODAK

STUDY COMPLETION DATE

October 7, 1996

n-BUTYL ACETATE

**A THIRTEEN-WEEK SUBCHRONIC INHALATION
TOXICITY STUDY IN THE RAT**

**HAEL NO. 94-0305 KAN 900710
CAS NO. 000123-86-4**

ABSTRACT

Male and female Sprague-Dawley (SD) rats were exposed to concentrations of 0, 500, 1500, or 3000 ppm of n-butyl acetate for 6 hours per day, 5 days per week for 13 consecutive weeks. The time-weighted average analytical concentrations were within 10% of the target concentrations. The daily mean temperatures and relative humidity inside the chambers during exposure were 21.1 - 24.7°C and 36.7 - 68.7%, respectively.

No spontaneous mortality occurred during the study. Animals were observed for signs of toxicity prior to exposure, once per hour during exposure, and 30 minutes to one hour after exposure. Animals exposed to 3000 ppm had reduced activity levels which were of generally minor severity during exposure. Signs of sialorrhea and red discoloration on the chin hair were also observed. Animals exposed to 1500 ppm exhibited reduced activity of generally minimal severity. Control and 500 ppm animals appeared normal during exposure. After exposure, animals in all groups had porphyrin nasal discharges and dried porphyrin stains around the nose. These clinical signs were occasionally seen during the morning examination before exposure.

Mean body weights for the 3000 ppm group were significantly ($p \leq 0.05$) lower than the control group for male rats on Days 7, 14, 21, 28, 35, 42, 49, 56, 63, 70, 77, 84, and 91, and for female rats on Days 14, 21, 28, 35, 42, 56, 63, 70, 77, 84, and 91. Mean feed consumption for the 3000 ppm groups were significantly lower ($p \leq 0.05$) than for the control group throughout the study for male rats and at all intervals except Days 84 and 91 for female rats. Mean body weights for the male 1500 ppm group were significantly ($p \leq 0.05$) lower than the control group on Days 42, 49, 56, 63, 70, 77, 84, and 91. Mean body weights for the female 1500 ppm group were significantly ($p \leq 0.05$) lower than the control group on Days 14, 21, 28, 35, 42, 56, 63, 70, 77, 84, and 91. Mean feed consumption values for the 1500 ppm groups were significantly lower ($p \leq 0.05$) than for the control group on Days 35, 42, 49, 56, 63, 70, 77, and 84 for male rats and at all intervals except Day 91 for female rats. Mean body weights for the 500 ppm groups were comparable to the control group throughout the study, and no statistically significant differences were noted. However, mean feed consumption values for the 500 ppm groups were significantly lower ($p \leq 0.05$) than for the control group on Days 35, 42, 63, and 70, for male rats and on Days 7 and 14 for female rats.

Blood was collected from 5 animals per group after 30 days of exposure, and from 10 animals per group at termination. No significant differences in hematologic parameters were