

Benzyl acetate

NAME OF **SUBSTANCE** **BENZYL ACETATE**
CAS **REGISTRY** NUMBER 140-114

TOXIC HAZARD RATING

No data are available in humans. Limited evidence of carcinogenicity in animals. **OVERALL EVALUATION:** Group 3: The agent is not classifiable as to its carcinogenicity to humans. [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). S7 58 (1987)] ****PEER REVIEWED****

HUMAN TOXICITY EXCERPTS

IF INGESTED CAN CAUSE GI IRRITATION WITH VOMITING & DIARRHEA. [Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989. , p. 176] ****PEER REVIEWED****

HUMAN TOXICITY EXCERPTS

... BENZYL ACETATES . . . ARE OF LOW VOLATILITY . . . & EXCEPT FOR LOCAL IRRITATION, NO EFFECTS HAVE BEEN REPORTED IN MAN. [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1864] **"PEER REVIEWED**"**

HUMAN TOXICITY EXCERPTS

SUMMARY TOXICITY STATEMENT: ACUTE= HIGH VIA INHALATION ROUTE. HIGH= CAPABLE OF CAUSING DEATH OR PERMANENT INJURY DUE TO EXPOSURES OF NORMAL USE; INCAPACITATING & POISONOUS; REQUIRES SPECIAL HANDLING. [Sax, N.I. Dangerous Properties of Industrial Materials. 5th ed. New York: Van Nostrand Rheinhold, 1979, , p. 409] **"PEER REVIEWED**"**

HUMAN TOXICITY EXCERPTS

SUMMARY TOXICITY STATEMENT; ACUTE= MODERATE VIA ORAL ROUTE. AN IRRITANT. MODERATE= MAY CAUSE REVERSIBLE OR IRREVERSIBLE CHANGES TO EXPOSED TISSUE, NOT PERMANENT INJURY OR DEATH; CAN CAUSE CONSIDERABLE DISCOMFORT. [Sax, N.I. Dangerous Properties of Industrial Materials. 5th ed. New York: Van Nostrand Rheinhold, 1979. , p. 409] **"PEER REVIEWED**"**

HUMAN TOXICITY EXCERPTS

Benzyl acetate produces respiratory tract irritation and narcotic effects in humans, and **continued** exposure to benzyl acetate at an ambient concentration of 50 ppm results in kidney damage. **When ingested,** benzyl acetate can cause general intestinal irritation. [DHHS/NTP; Toxicology and Carcinogenesis Studies of Benzyl acetate in **F344/N** Rats and **B6C3F1** Mice (Gavage Studies) **p.19** (1986) Technical Rpt Series No. 250 NIH Pub No. **86-2506**] ****PEER REVIEWED****

NON-HUMAN TOXICITY EXCERPTS

MICE EXPOSED TO 212 PPM FOR 7-13 HR: RESULTS INCL DYSPNEA; NARCOSIS; DEATH. /FROM TABLE/ [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1863] ****PEER REVIEWED****

NON-HUMAN TOXICITY EXCERPTS

CATS EXPOSED TO 180 PPM 8-9 HR FOR 7 DAYS: RESULTS IN IRRITATION; GRADUAL WEAKNESS; LOSS OF APPETITE & WEIGHT; DROWSINESS; DEATH. /FROM TABLE/

[Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1863] "PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

... IN MODERATE CONCN VAPOR IS RATHER IRRITATING TO EYES. DISCOMFORT TENDS TO DIMINISH DURING CONTINUED EXPOSURE. TESTING BY APPLICATION OF DROP OF LIQUID TO EYES OF RABBITS CAUSED IMMEDIATE BLEPHAROSPASM FOR ... MINUTE DESPITE PREVIOUS APPLICATION OF LOCAL ANESTHETIC. CORNEAS WERE FOUND NOT TO BE DAMAGED. {Grant, W. M. Toxicology of the Eye. 2nd ed. Springfield, Illinois: Charles C. Thomas, 1974. , p. 183} **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

ORAL, SC & IP ADMIN HAS CAUSED CENTRAL NERVOUS PARALYSIS IN RABBITS, & ORAL ADMIN DIURESIS. REPEATED EXPOSURE TO ITS VAPOR HAS CAUSED ALBUMINURIA ... CONSIDERED TO BE INDICATION OF KIDNEY INJURY. [Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. , p. 544] "PEER REVIEWED**"

NON-HUMAN TOXICITY EXCERPTS

ANIMALS SUBJECTED TO LETHAL ORAL DOSAGE SHOWED SLIGHT EDEMA OF LUNGS. ANIMALS KILLED AFTER REPEATED INHALATION SHOWED SLIGHT TRACHEITIS & BRONCHITIS. KIDNEYS SOME HYPEREMIA. [Browning, E. Toxicity and Metabolism of Industrial Solvents. New York: American Elsevier, 1965. , p. 544] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

Benzyl acetate was found to be negative when tested for mutagenicity using the Salmonella/microsome preincubation assay, using the standard protocol approved by the National Toxicology Program (NTP). Benzyl acetate was tested in as many as 5 Salmonella typhimurium strains (TA1535, TA1537, TA97, TA98, and TA100) in the presence and absence of rat and hamster liver S9, at doses of 0.033, 0.100, 0.333, 1.000, 3.333, and 10.000 mg/plate. The highest ineffective dose tested in any Salmonella typhimurium strain was 10.000 mg/plate. [Mortelmans K et al; Environ Mutagen 8: 1-19 (1986)] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

Benzyl acetate gave negative results in an assay for differential killing of repair proficient and deficient strains of Bacillus subtilis H17 and M45, and it was not mutagenic in strains TA1535, TA1537, TA98, or TA100 of Salmonella in the presence or absence of Aroclor 1254-induced rat liver S9. In tests performed by the NTP, neither benzyl acetate nor benzyl alcohol was mutagenic in Salmonella in the presence or absence of Aroclor 1254-induced Sprague Dawley rat or Syrian hamster liver S9. In cultured Chinese hamster ovary cells, benzyl acetate did not induce sister chromatid exchanges or chromosomal aberrations. Benzyl acetate was mutagenic in the L5178Y/TK + or - mouse lymphoma assay in the presence, but not in the absence, of Aroclor 1254-induced rat liver S9. Benzyl acetate did not induce unscheduled DNA synthesis in Fischer 344 rat hepatocytes following in vivo and in vitro treatment. [DHHS/NTP; Toxicology and Carcinogenesis Studies of Benzyl Acetate in F344/N Rats and B6C3F1 Mice (Gavage Studies) p.19 (1986) Technical Rpt Series No. 250 NIH Pub No. 86-2506] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

Urine flow in dogs and rabbits increased approximately 180% two hours after they received an

ip injection of 0.4 ml/kg body weight. [DHHS/NTP; Toxicology and Carcinogenesis Studies of Benzyl Acetate in F344/N Rats and B6C3F1 Mice (Gavage Studies) p. 18 (1986) Technical Rpt Series No. 250 NIH Pub No. 86-2506] "PEER REVIEWED"

NON-HUMAN TOXICITY VALUES

Rat (Osborne-Mendel) oral 2.49 g/kg [DHHS/NTP; Toxicology and Carcinogenesis Studies of Benzyl Acetate in F344/N Rats and B6C3F1 Mice (Gavage Studies) p.18 (1986) Technical Rpt Series No. 250 NIH Pub No. 86-2506] "PEER REVIEWED**"

NATIONAL TOXICOLOGY PROGRAM REPORTS

Benzyl acetate >99% pure was administered in corn oil by gavage to groups of 50 male and 50 female F344/N rats at doses of 0, 250, or 500 mg/kg body weight and to groups of 50 male and 50 female B6C3F1 mice at doses of 0, 500, or 1000 mg/kg once daily five days per week for 103 weeks. The absence of any observable adverse effect of benzyl acetate on the survival or mean body weight gains of the rats or mice in the 2 year studies suggests that both the rats and the mice of each sex could have tolerated higher doses. An infection in the genital tract was probably responsible for the deaths of 26/35 control, 14/32 low dose, and 8/20 high dose female mice before the end of the study. Acinar cell adenomas in the pancreas of male rats occurred with a positive trend ($p < 0.01$), and the incidence in the high dose group (37/49, 76%) was significantly ($p < 0.01$) higher than in the vehicle controls (22/50, 44%). The incidence of these tumors in the low dose group (27/50, 54%) was comparable to that in the gavage controls. Acinar cell hyperplasia of the pancreas was observed in 37/50 control, 34/50 low dose, and 36/49 high dose male rats. No acinar cell hyperplasia or adenoma of the pancreas was observed in female rats. The incidence of retinopathy and cataracts in the high dose male rats was increased compared with the controls (retinopathy: 1/50; 0/50; 0/50; 20/50; cataracts: 0/50; 0/50; 13/50). Low dose female rats had an increased incidence of retinopathy (18/50).

Retinopathy and cataracts in rats have been associated with proximity to fluorescent light in this and previous studies. Preputial gland neoplasms occurred with a positive trend ($p < 0.05$) in male rats (cystadenocarcinoma: 0/50; 0/50; 3/50; all adenocarcinoma; 0/50; 1/50; 4/50; adenocarcinoma or carcinoma combined; 1/50; 1/50; 6/50). However the incidence of all preputial gland tumors was not significantly elevated (2/50; 1/50; 6/50). For female rats the incidence of clitoral gland neoplasms was marginally increased (2/50; 0/50; 5/50).

Hepatocellular adenomas occurred in mice of each sex with statistically significantly positive trends (males: 0/50; 5/49; 15/50; females: 0/50; 0/50; 6/50), and the incidences in the high dose groups were greater than those in the controls (males: $p < 0.001$; females; $p < 0.05$).

Heptocellular carcinomas were marginally elevated in dosed male and high dose female mice (males: 10/50; 14/49; 12/50; females: 1/50; 0/50; 5/50). Squamous cell papillomas or carcinomas of the forestomach (uncommon neoplasms) occurred with a positive trend ($p < 0.05$) in male mice (4/49; 4/48; 11/49). The incidence of these tumors was also marginally ($p < 0.05$) increased in the high dose female mice (0/50; 0/50; 4/48). The incidences of these tumors in both the high dose male and the high dose female mice were considerably higher than the historical mm oil gavage control rates at this laboratory (males, 2/296, 0.7%; females, 2/297, 0.7%) and throughout the program (males, 14/1,070, 1.3%; females 3/1,073, 0.3%).

Forestomach hyperplasia occurred at increased incidences in dosed mice of either sex (males: 1/49, 7/48, 22/49; females: 1/50, 6/50, 17/48). These neoplasms and hyperplasia of the forestomach were probably related to administration of benzyl acetate. [DHHS/NTP; Toxicology and Carcinogenesis Studies of Benzyl acetate in F344/N Rats and B6C3F1 Mice (Gavage Studies) p-7 (1986) Technical Rpt Series No. 250 NIH Pub No. 86-2506] **PEER REVIEWED**

IARC SUMMARY AND EVALUATION

No data are available in humans. Limited evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is **not** classifiable as to its carcinogenicity to humans.

IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). S7 58 (1987)] "PEER REVIEWED"*

APPENDIX 8

**RESPIRATORY DEPRESSION VS. TIME FOR
INDIVIDUAL EXPOSURES TO TARGET COMPOUNDS AND MIXTURES**

FIGURE B-1

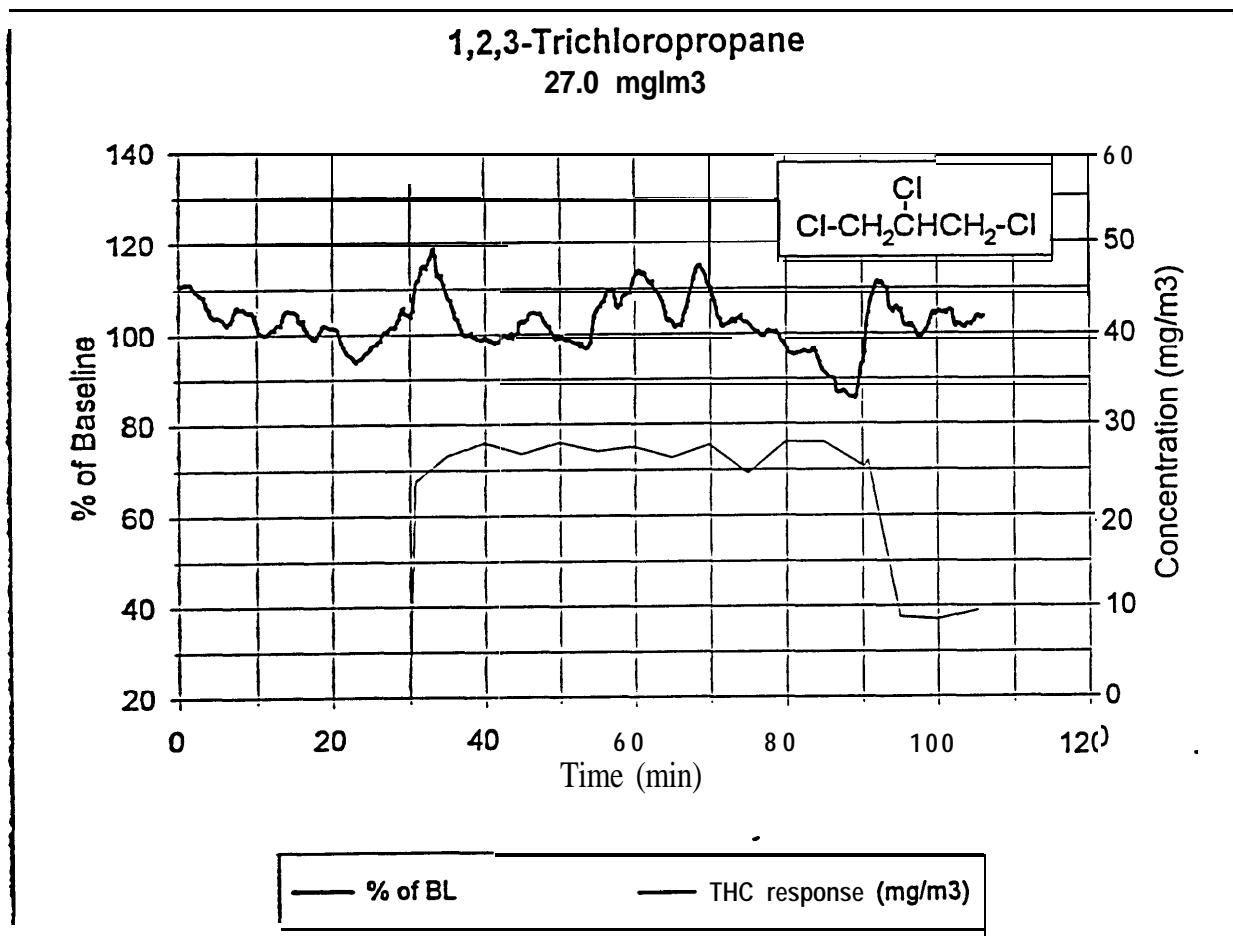


FIGURE B-2

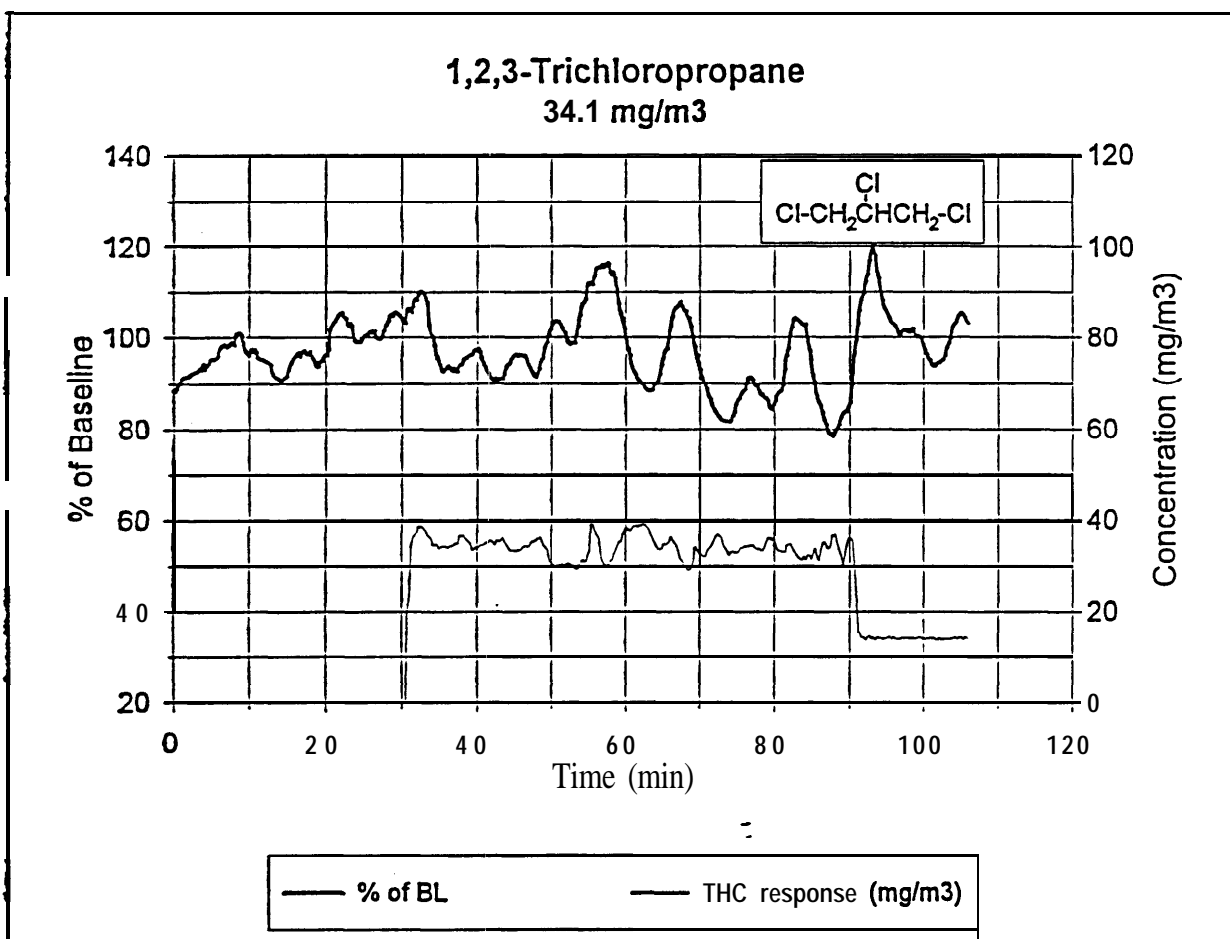
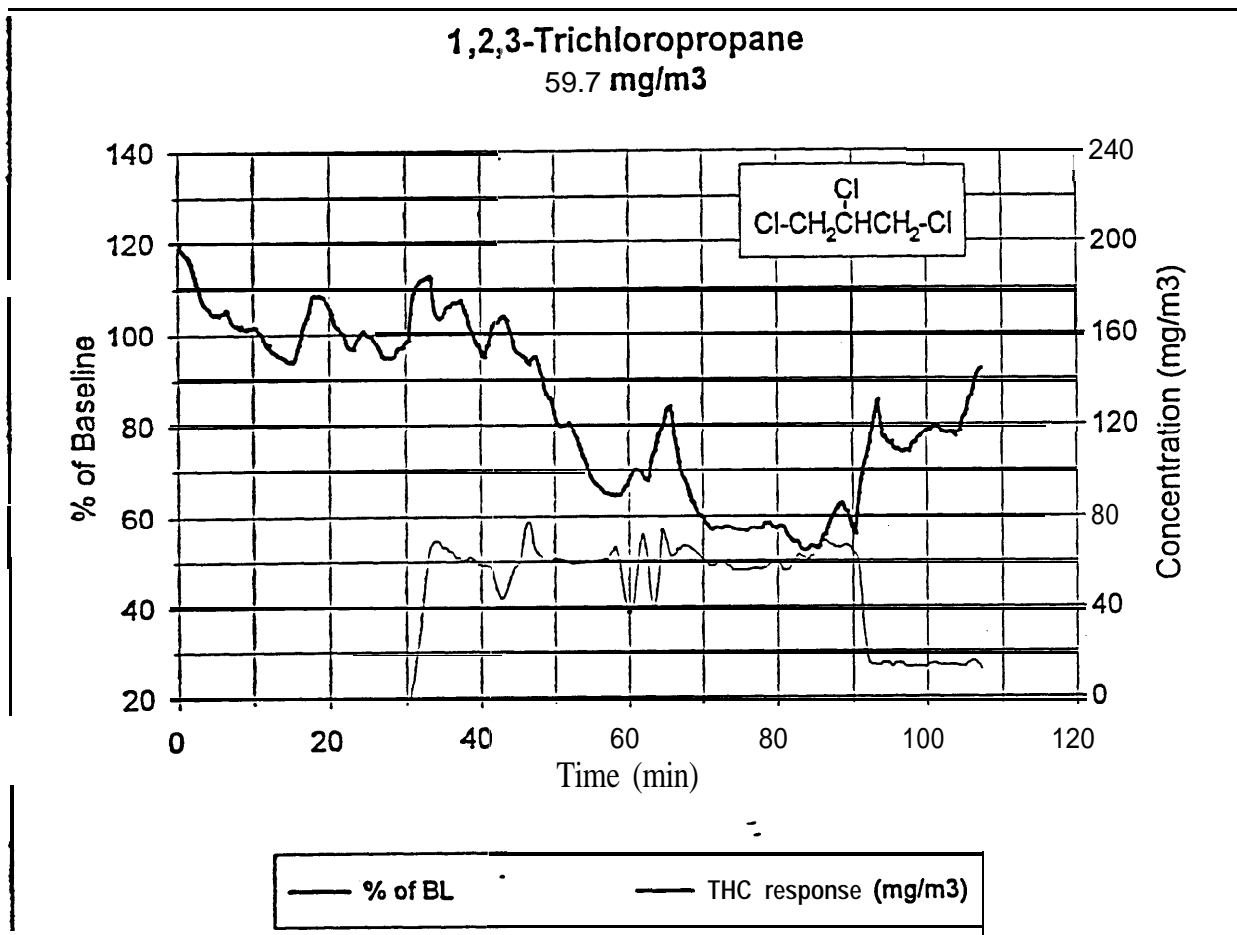


FIGURE B-4



FIGUREB-5

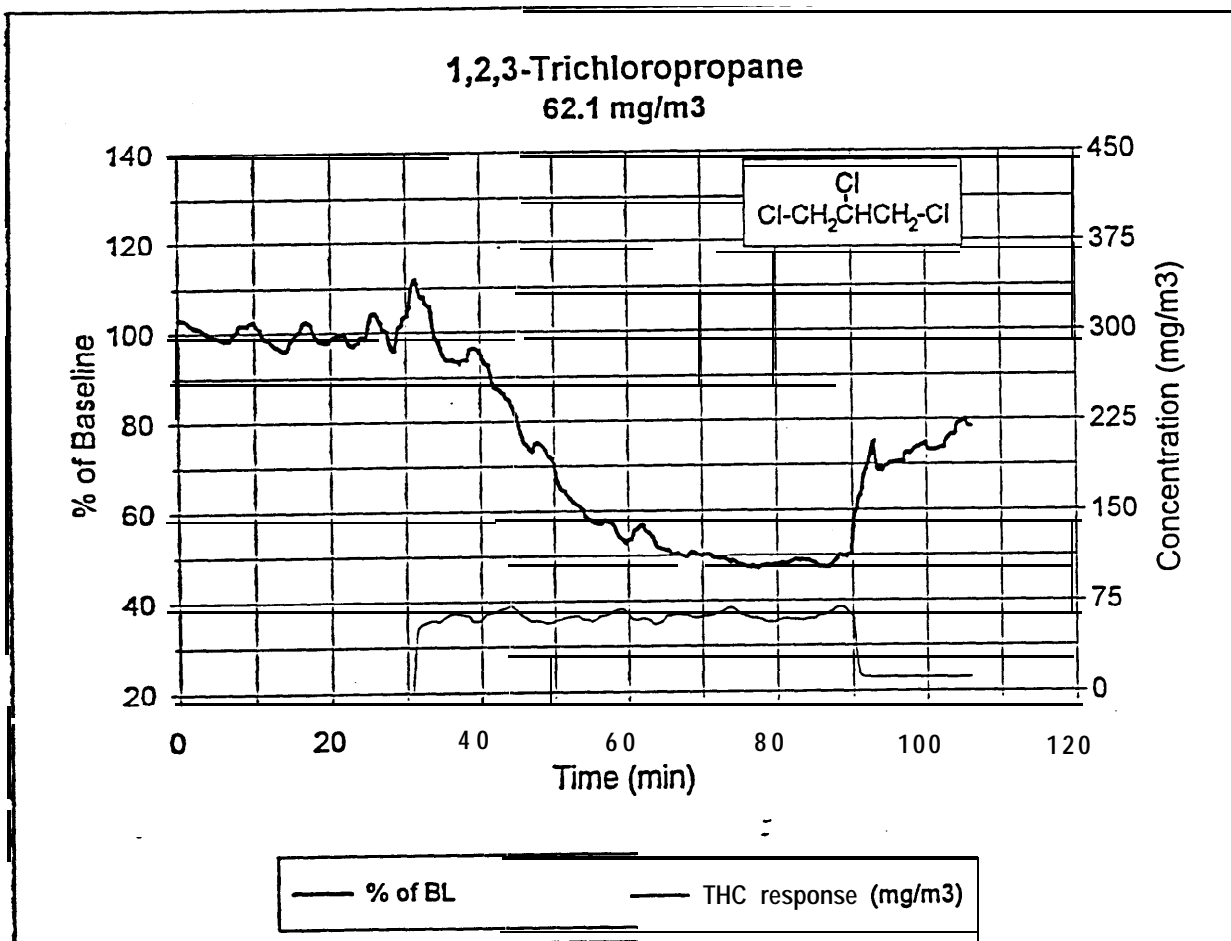


FIGURE B-6

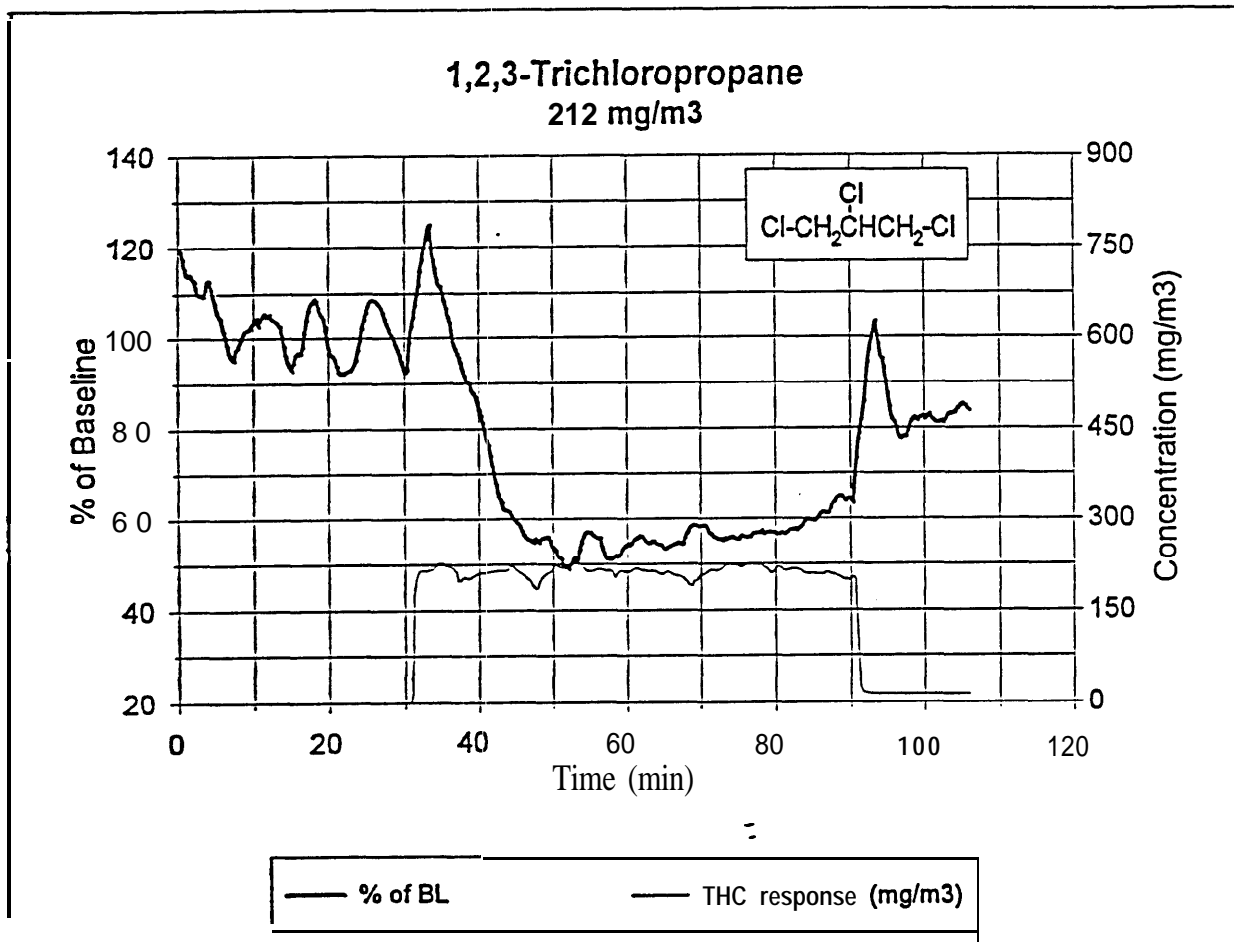


FIGURE B-7

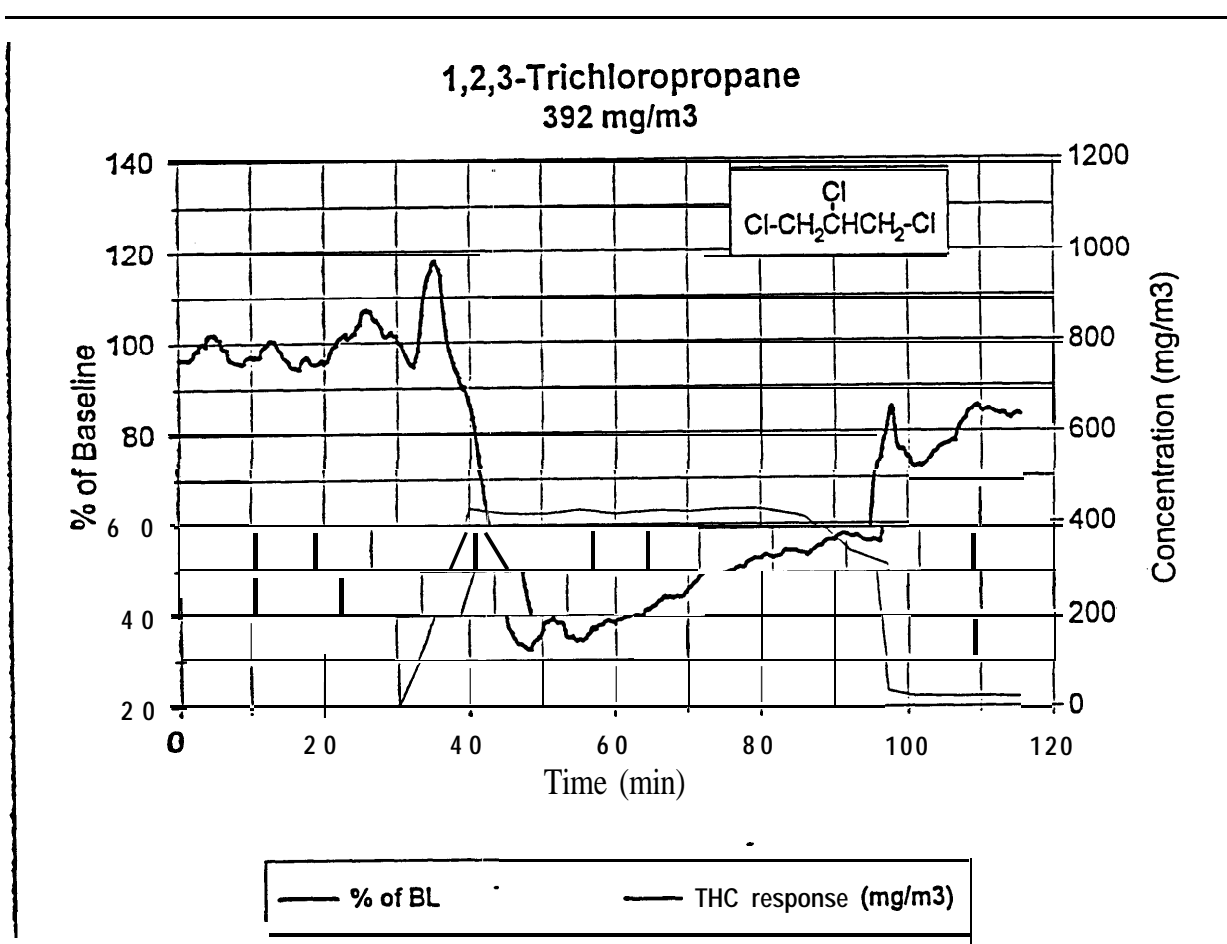


FIGURE B-8

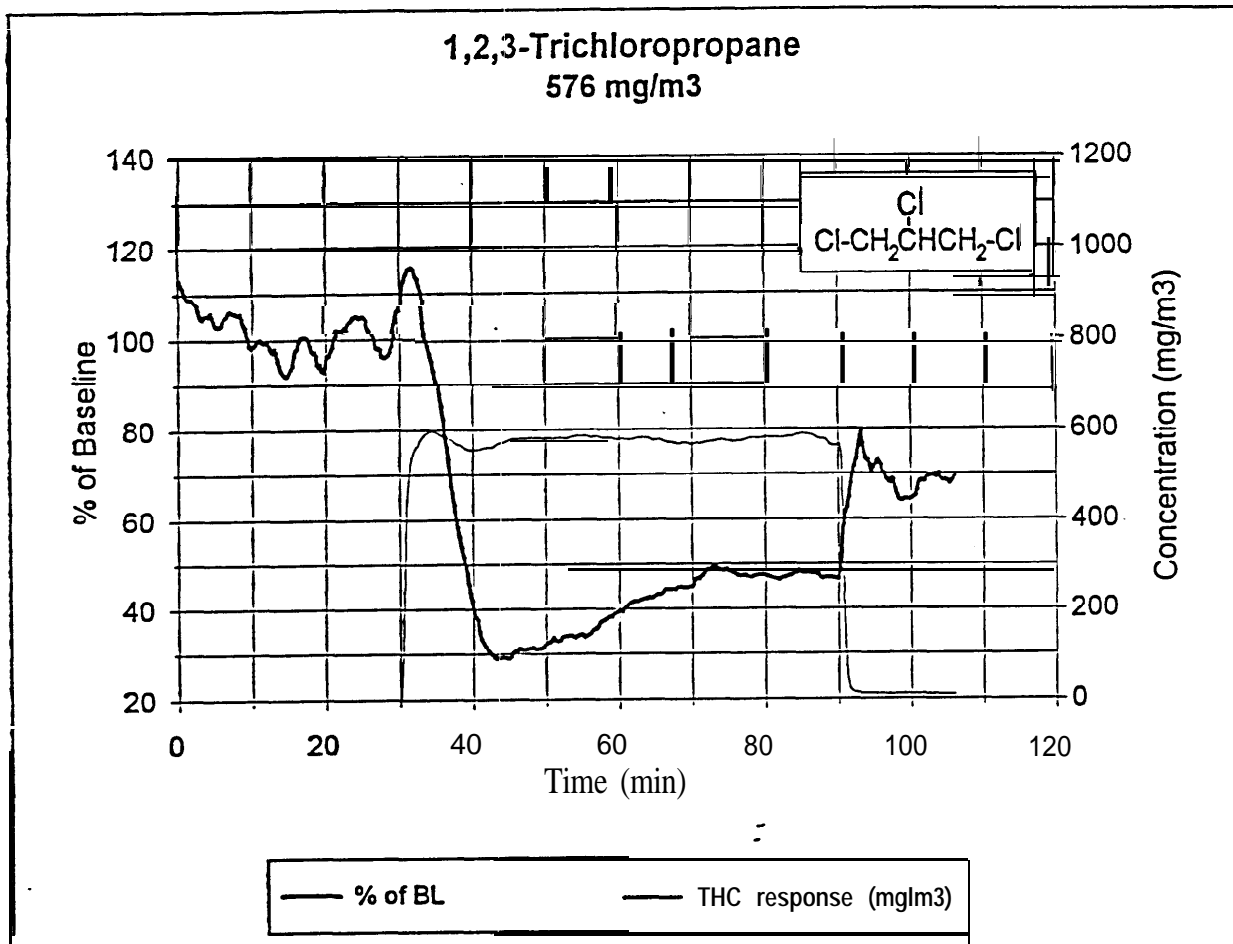


FIGURE B-9

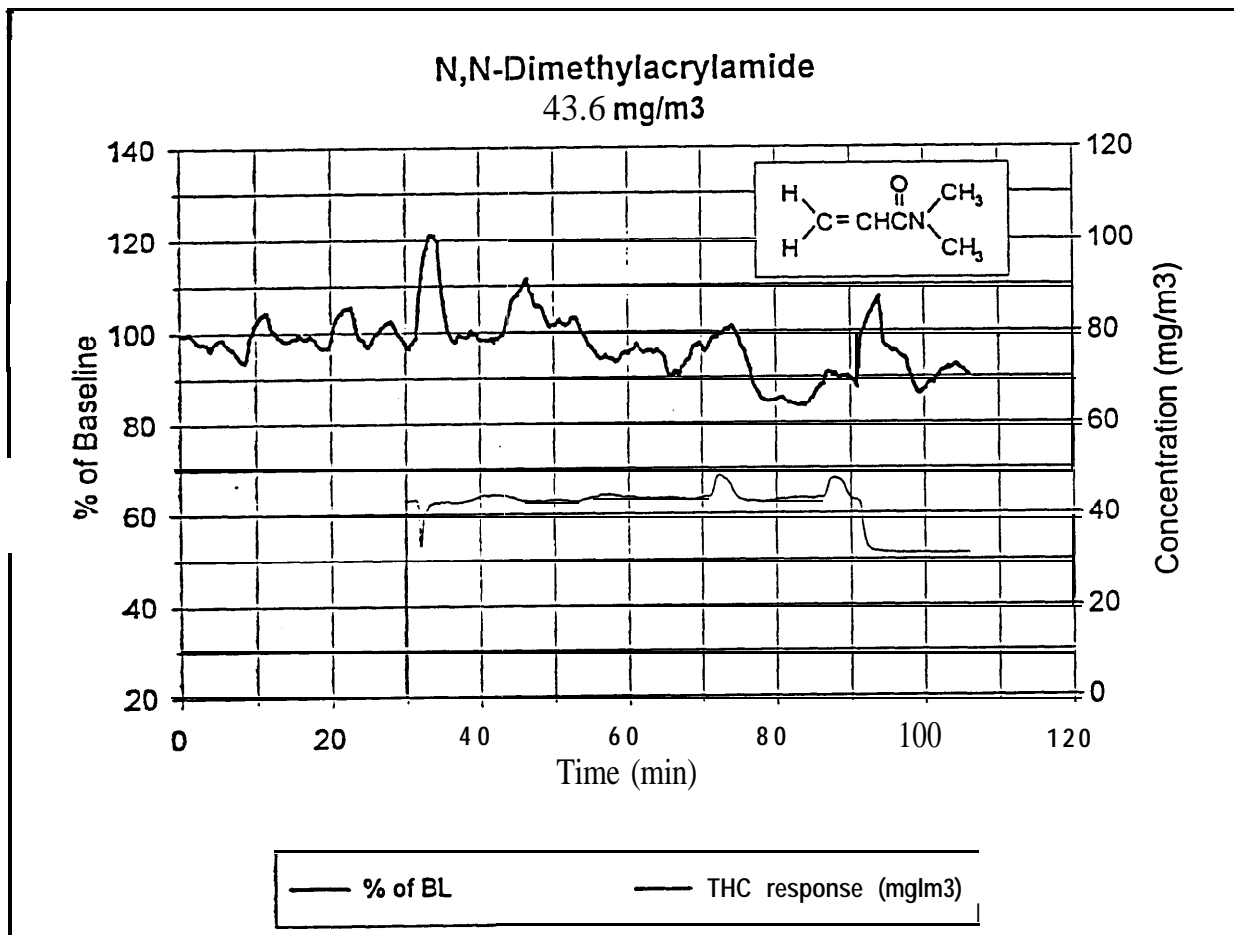


FIGURE B-10

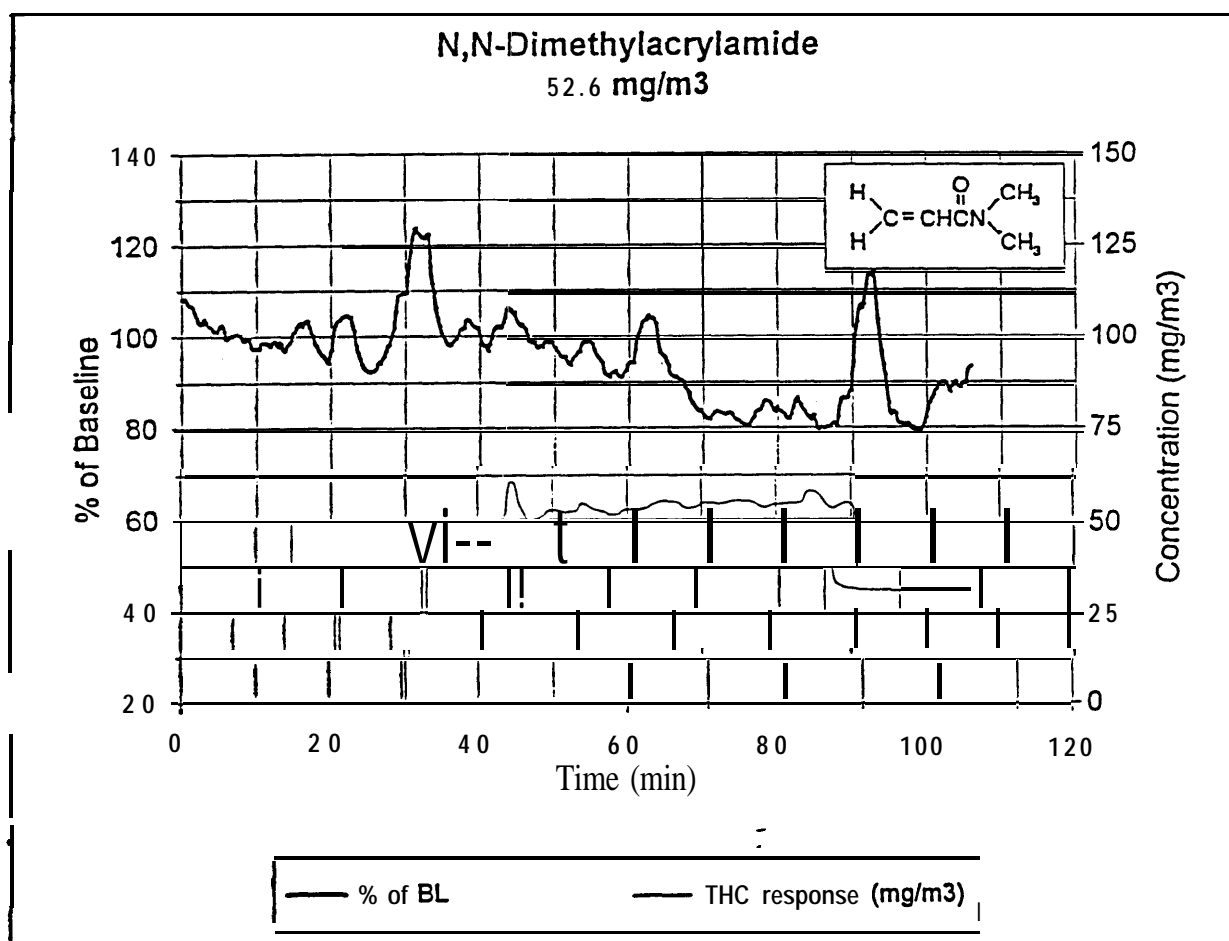


FIGURE B-1 1

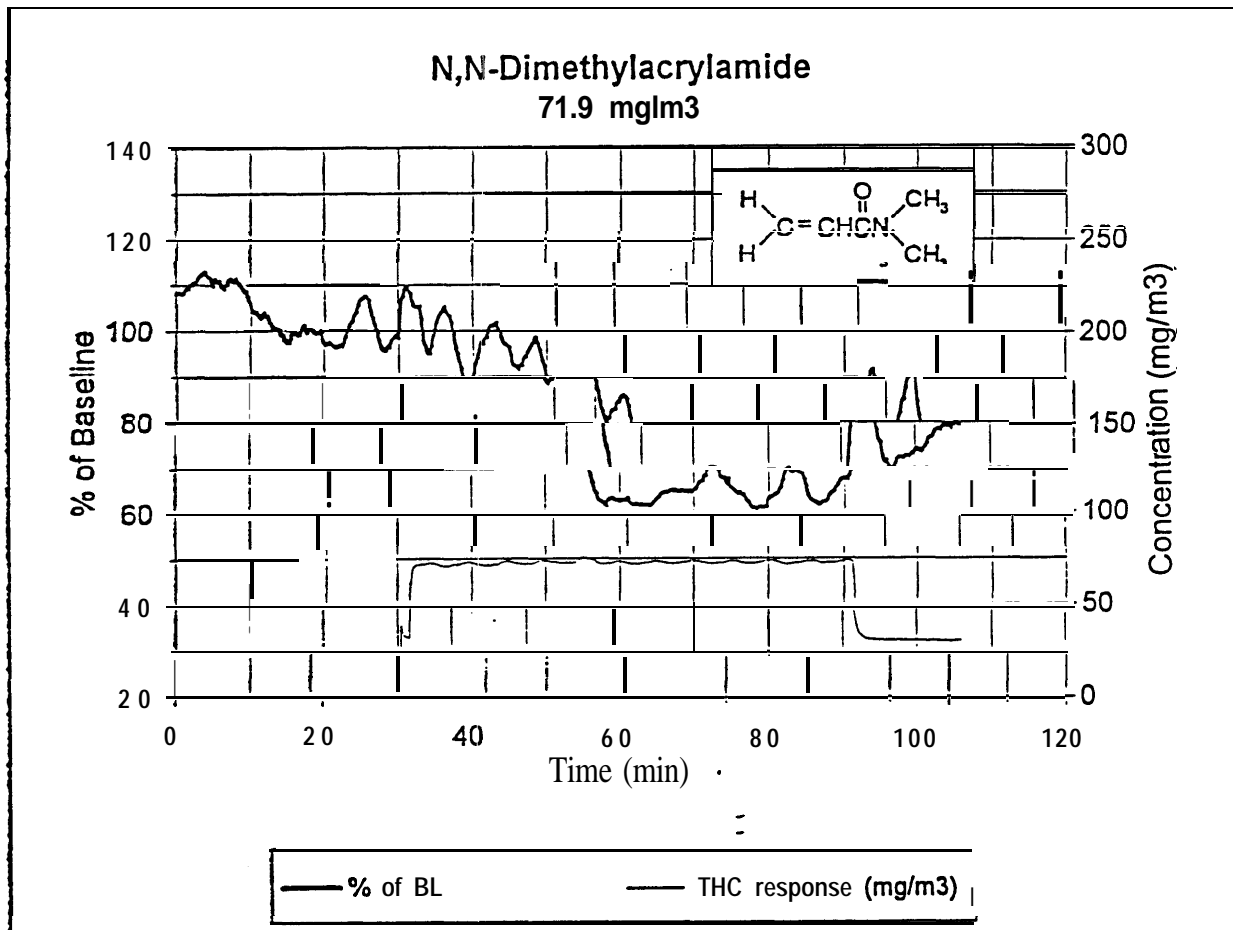


FIGURE B-12

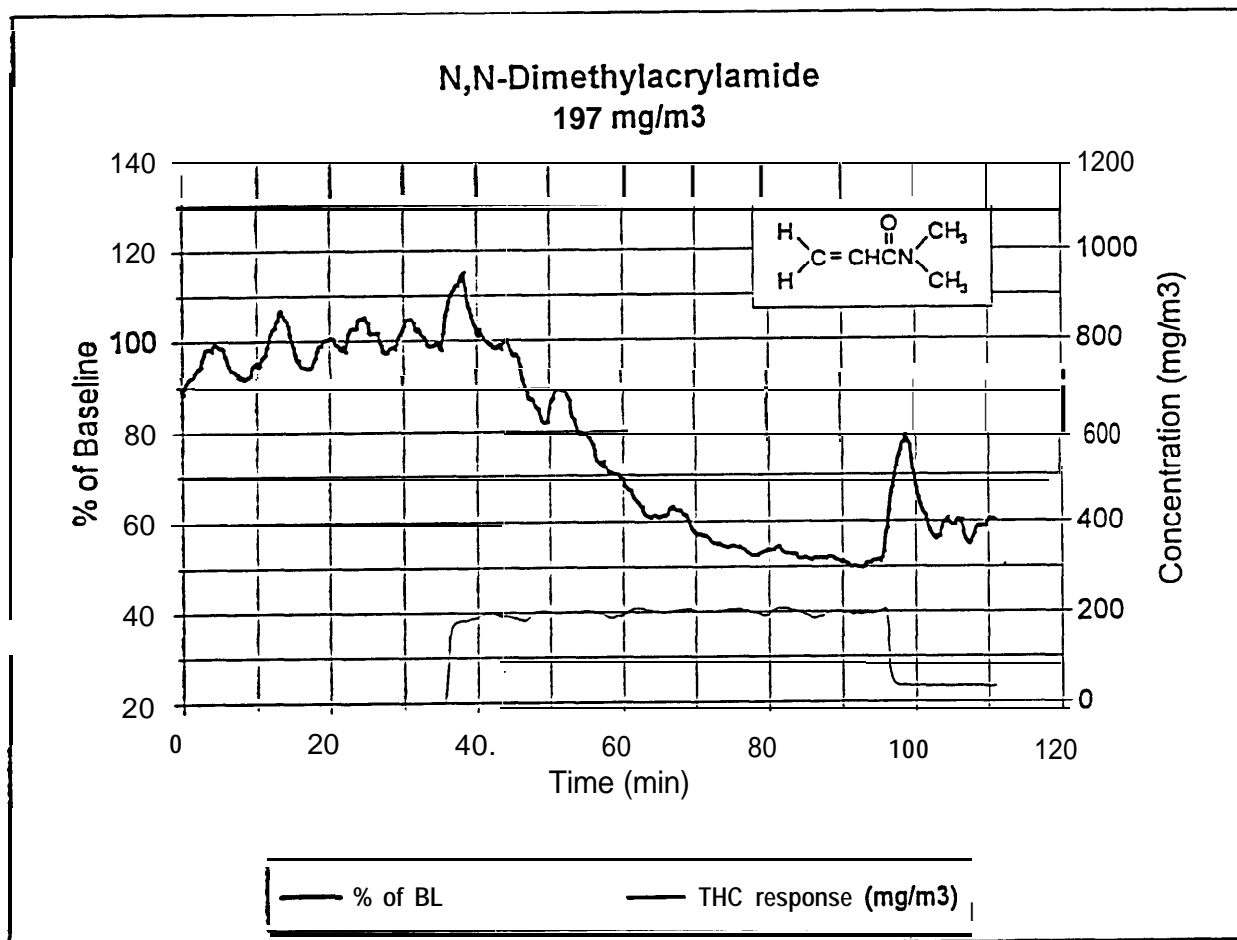


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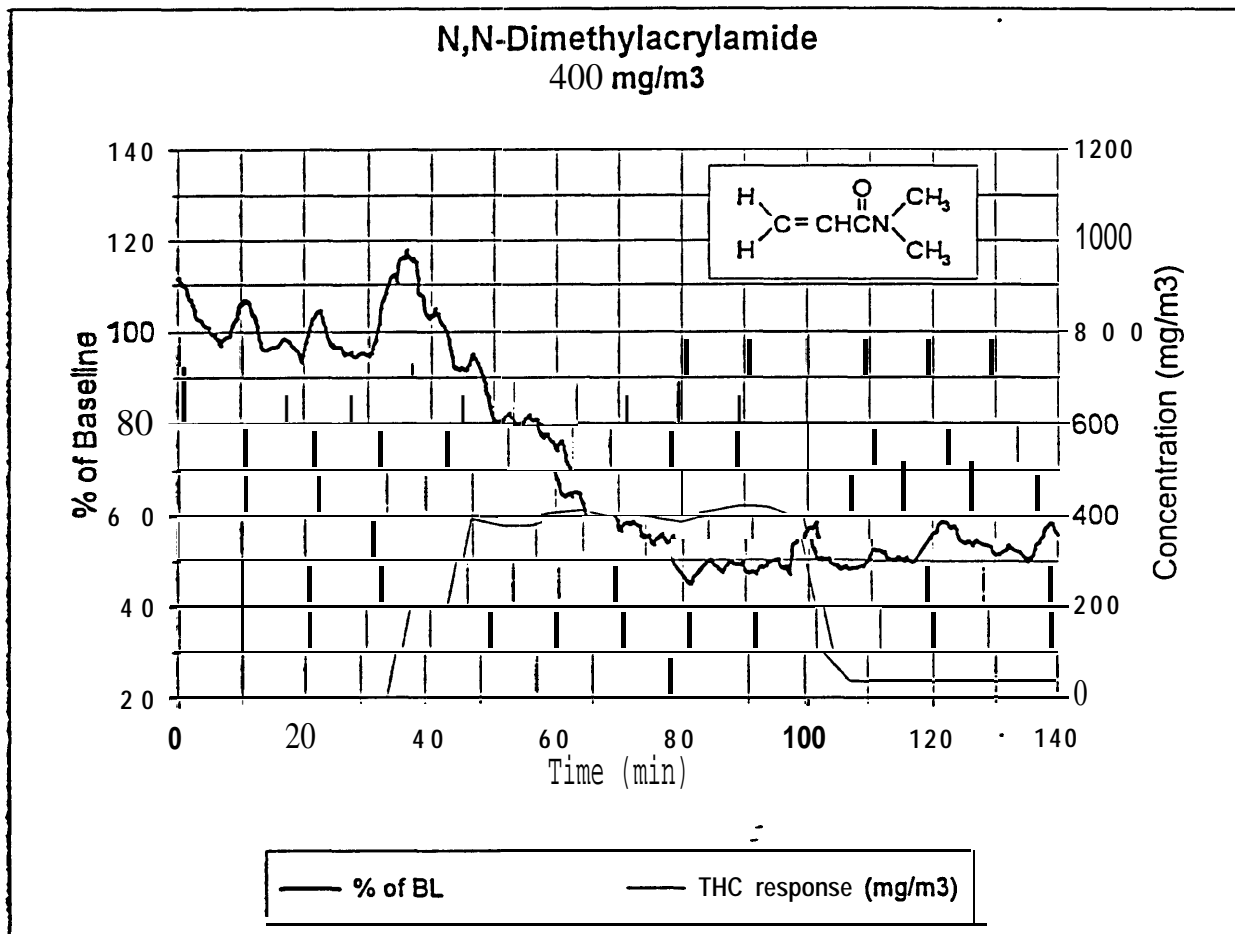


FIGURE B-14

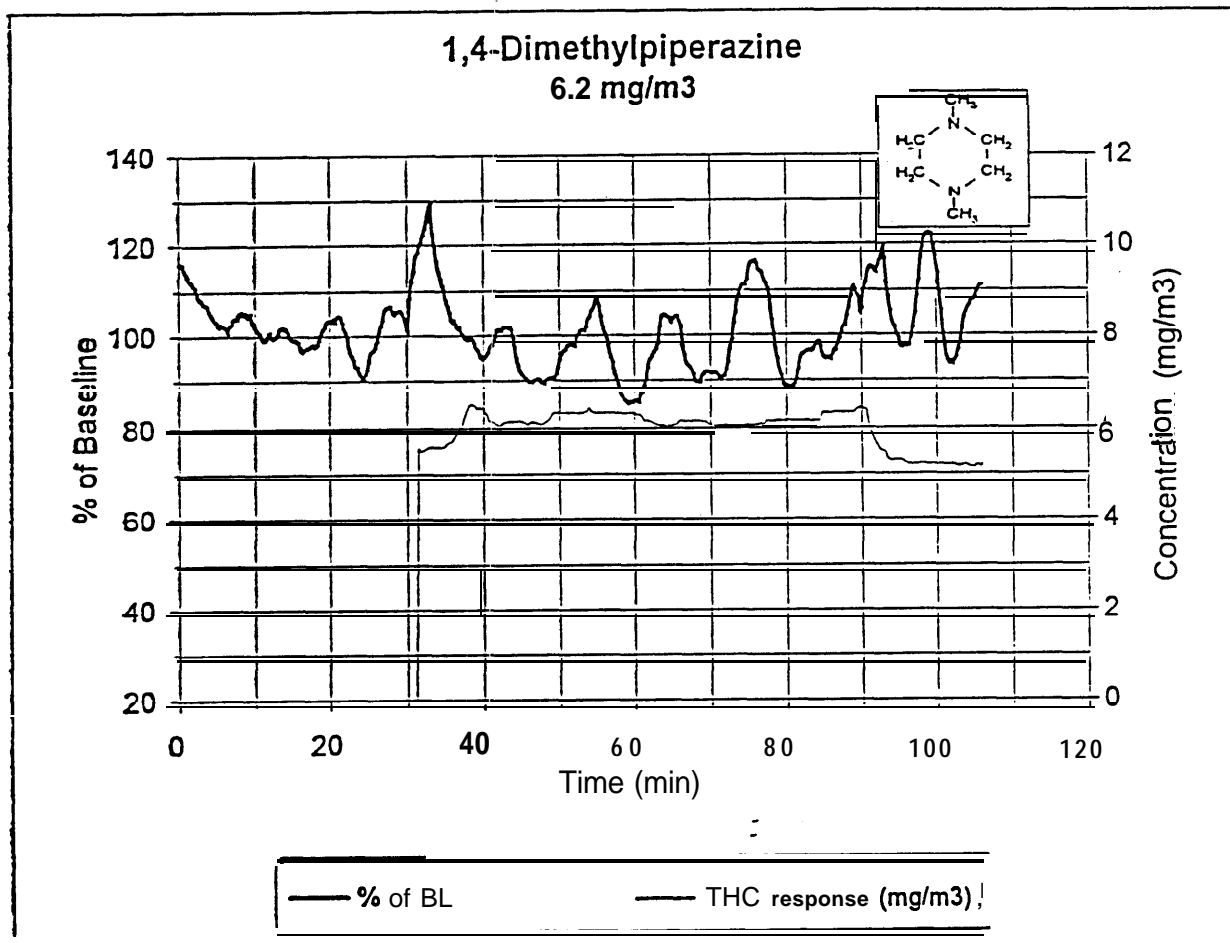


FIGURE B-1 5

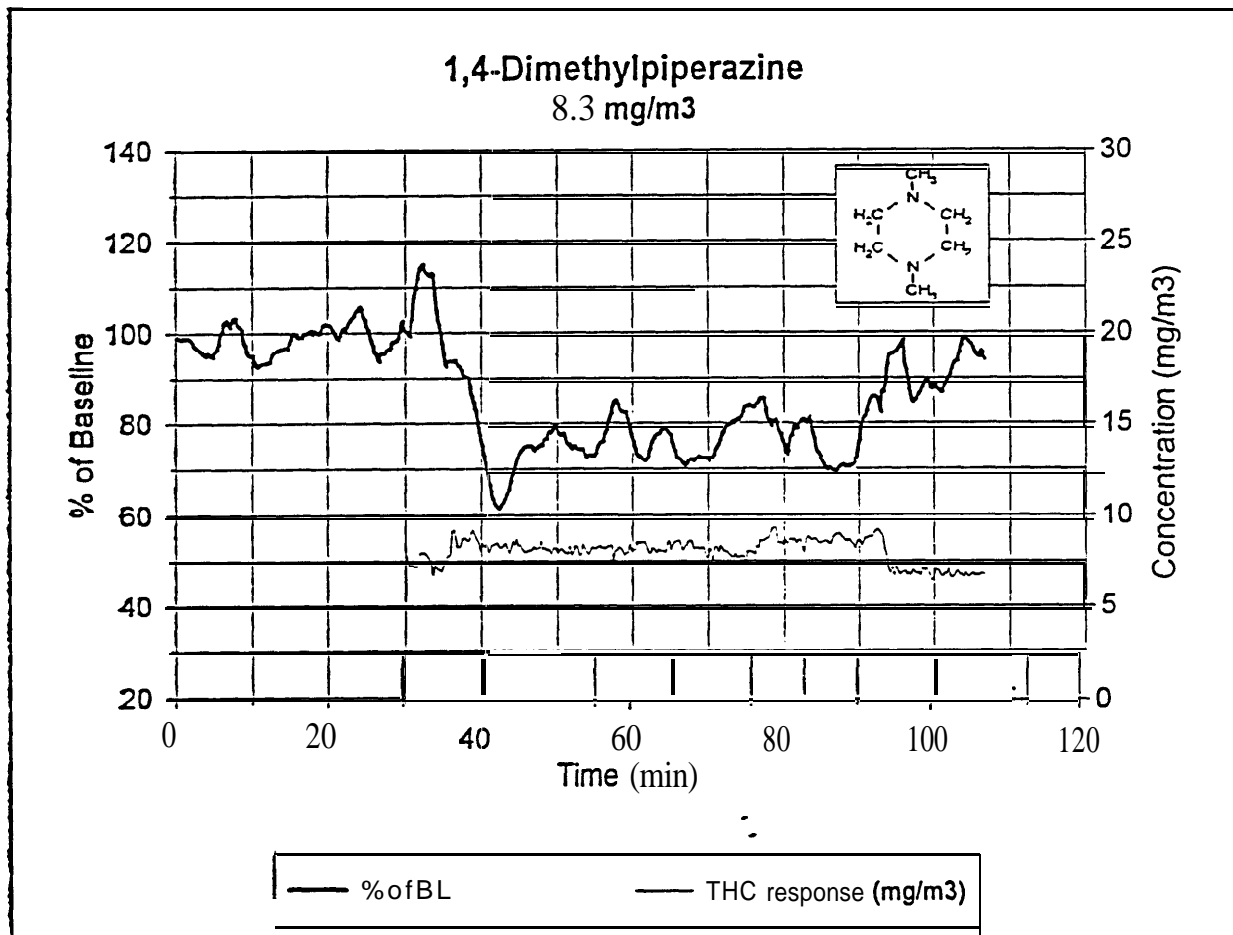


FIGURE B-1 6

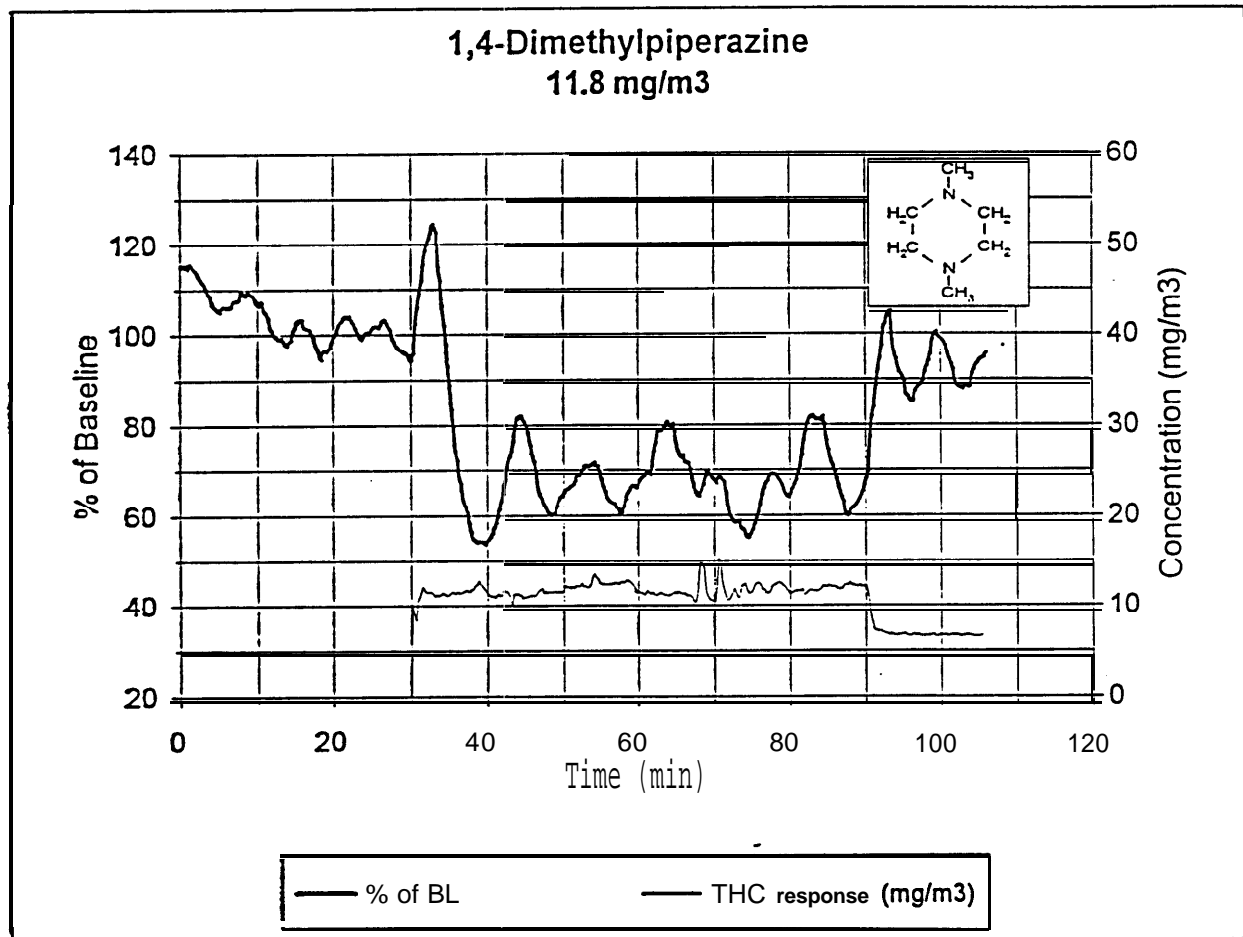


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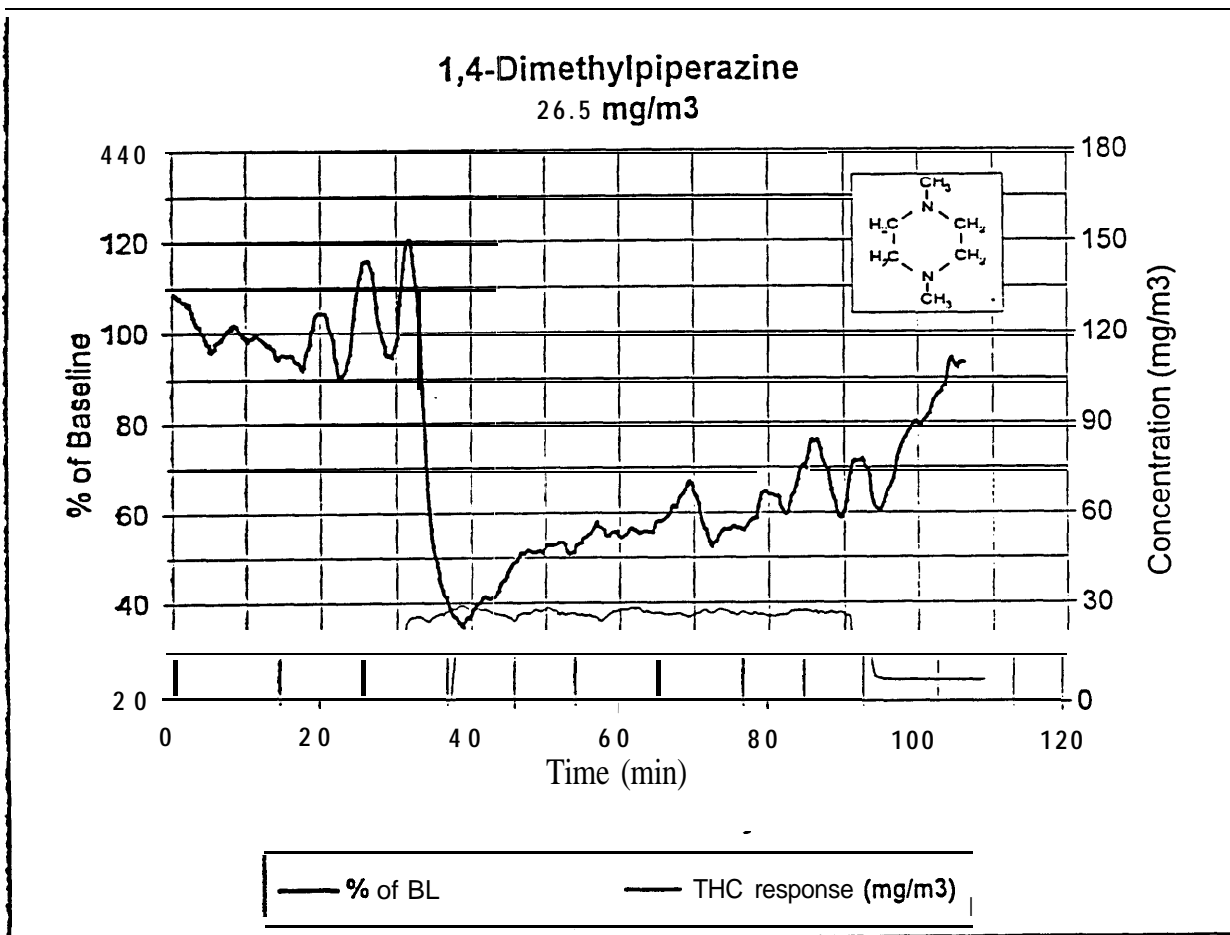


FIGURE B-I 8

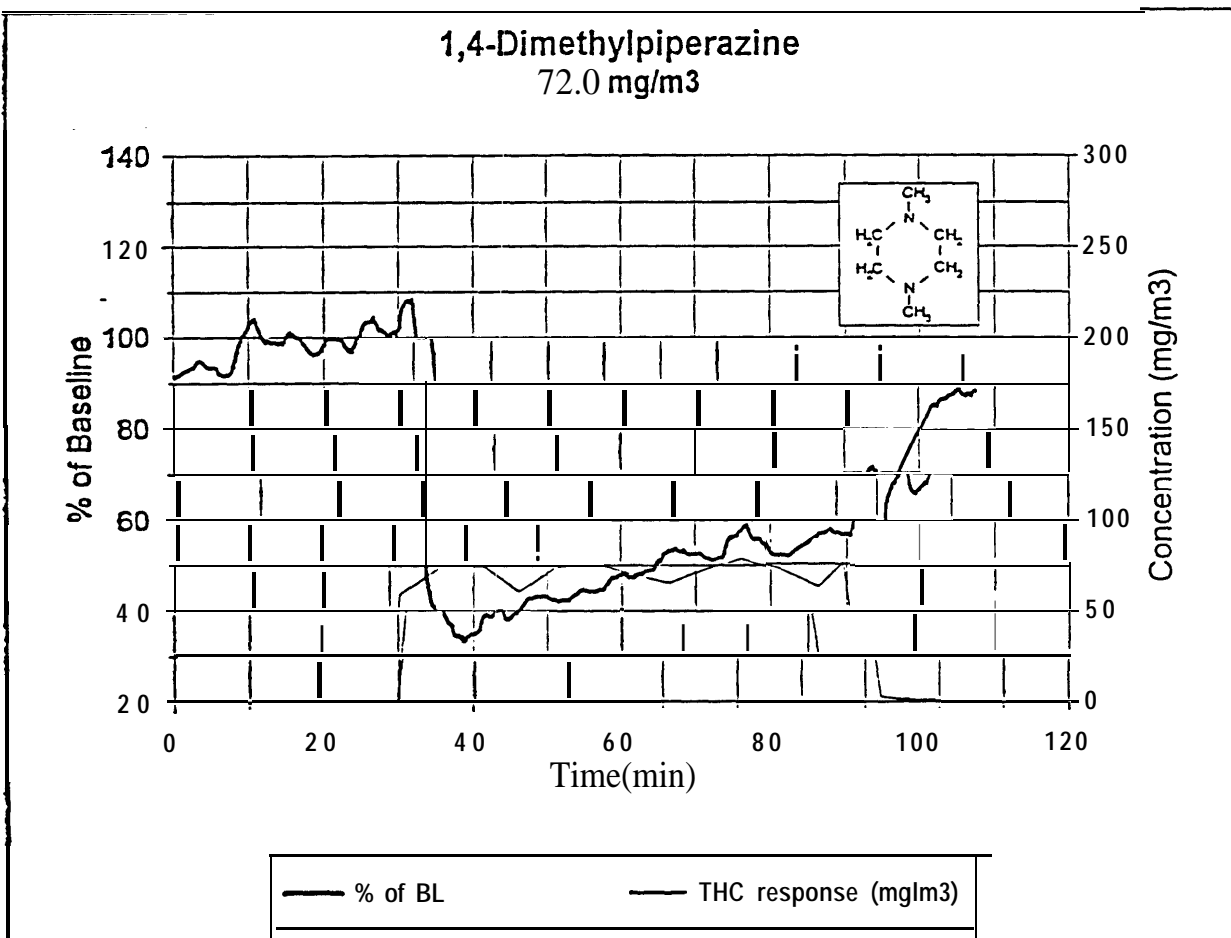


FIGURE B-I 9

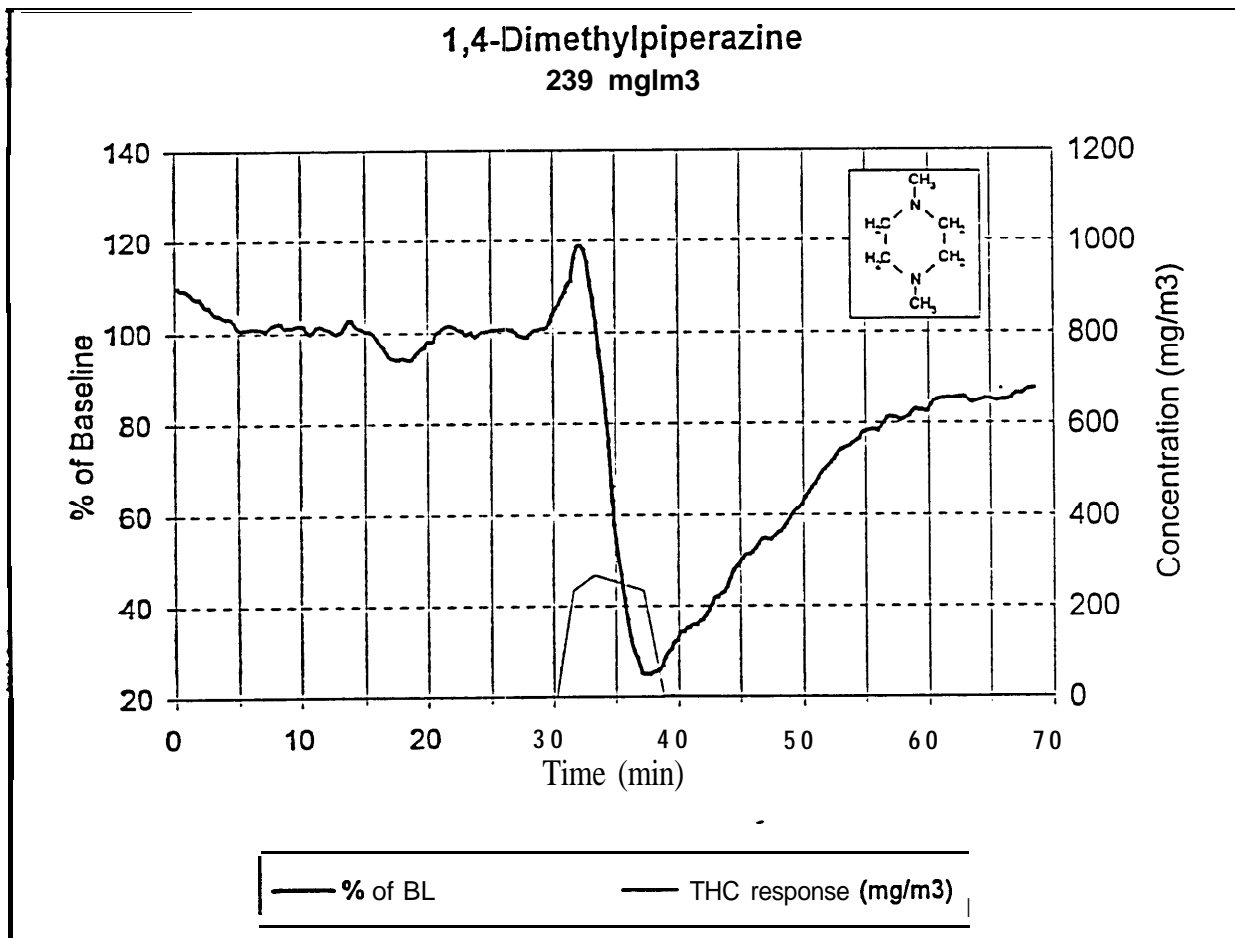


FIGURE B-20

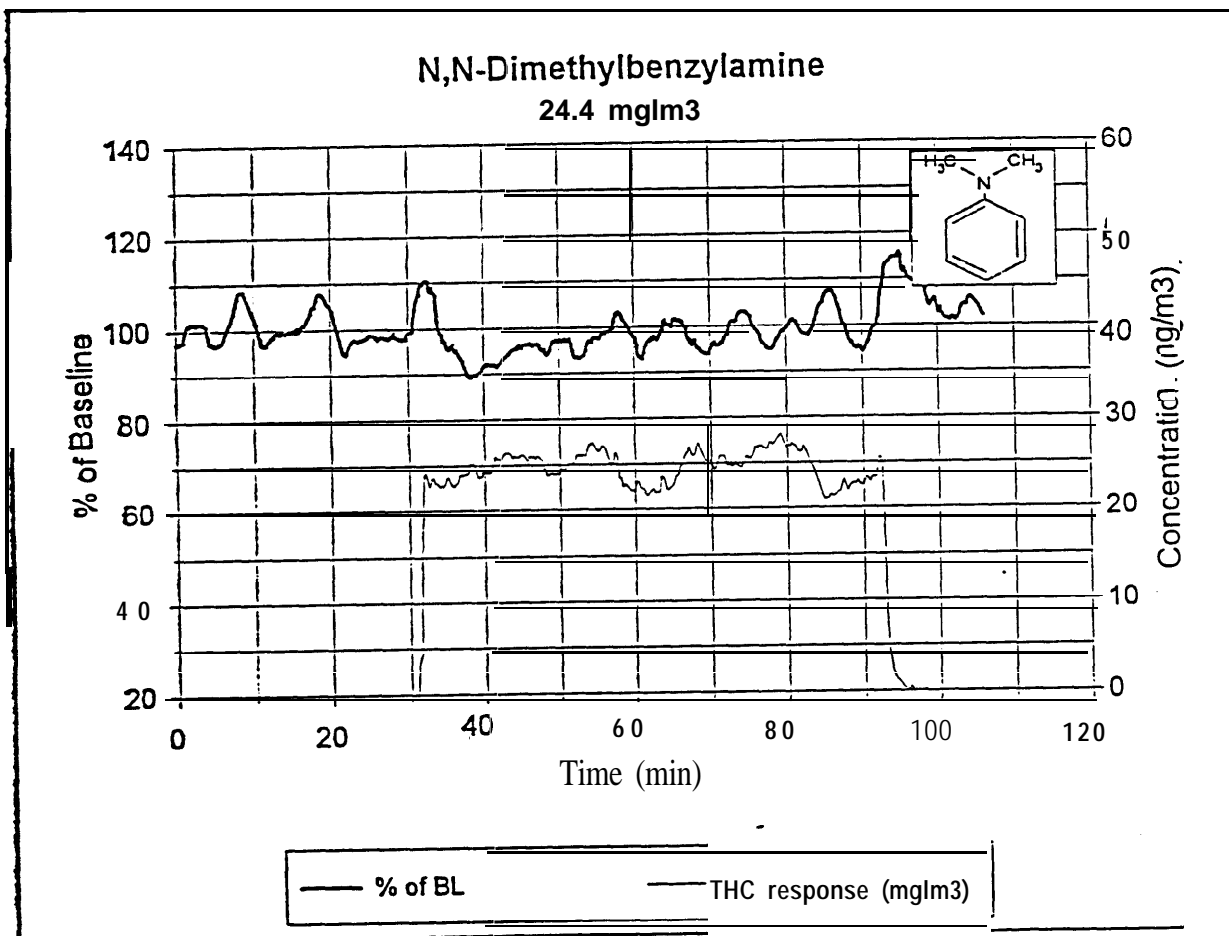


FIGURE B-21

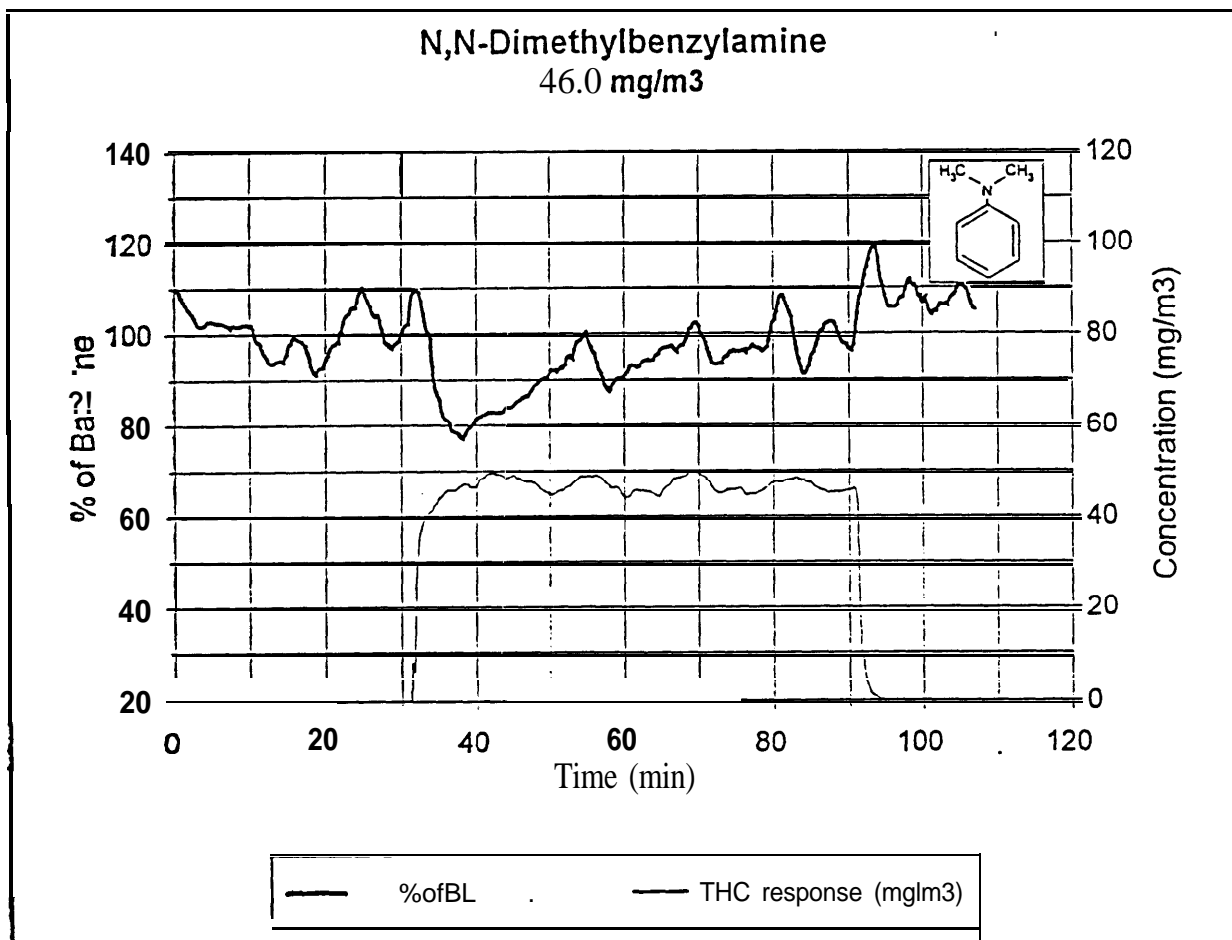


FIGURE B-22

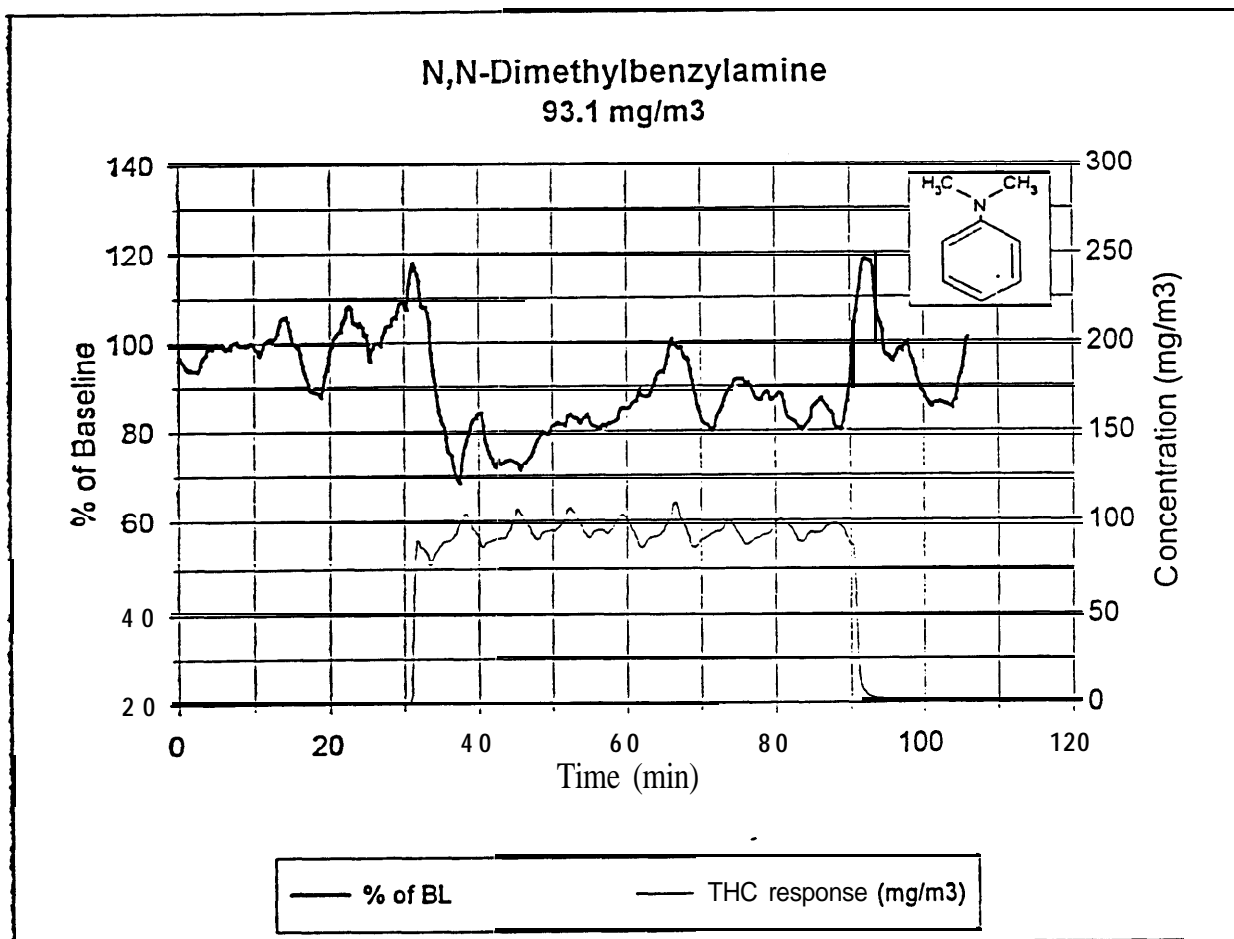


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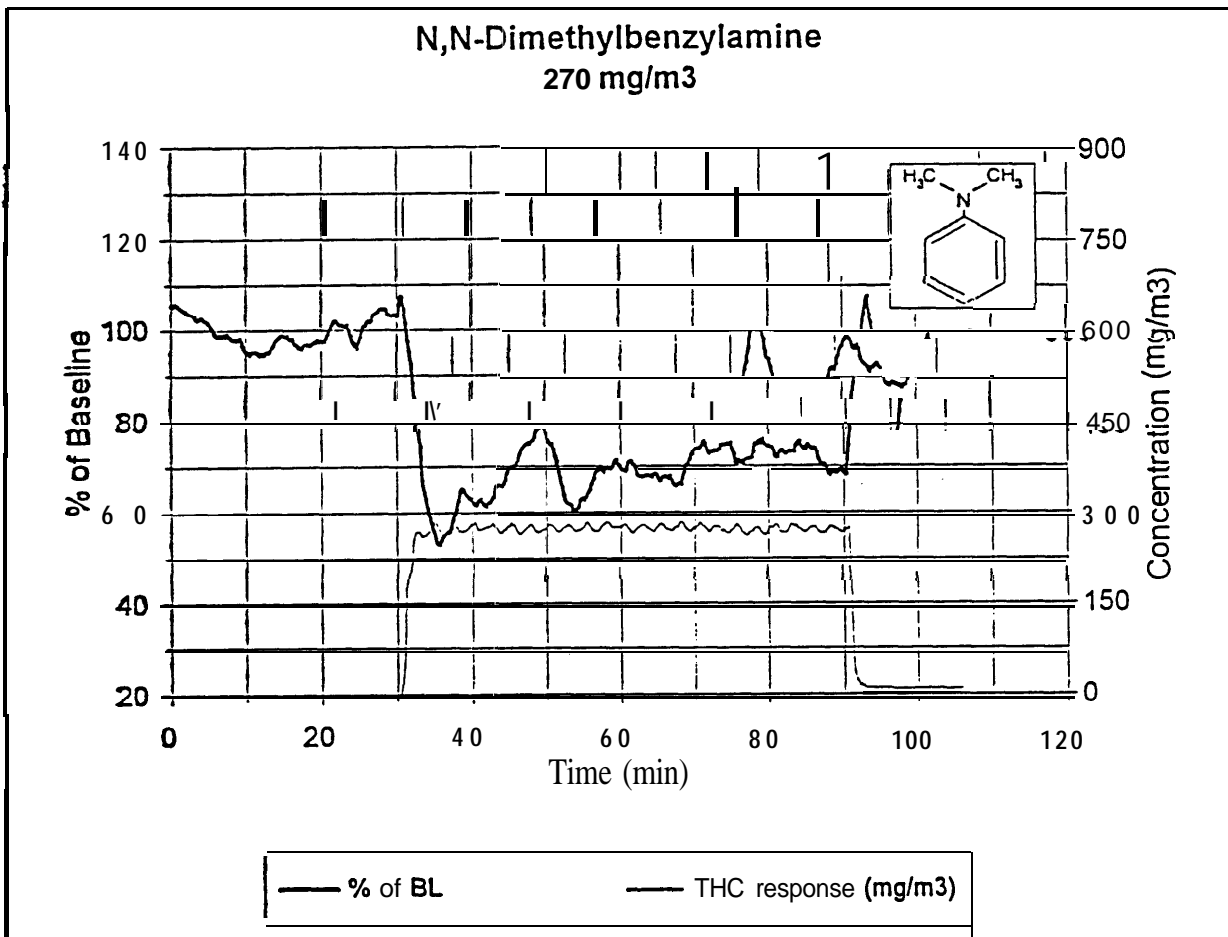


FIGURE B-24

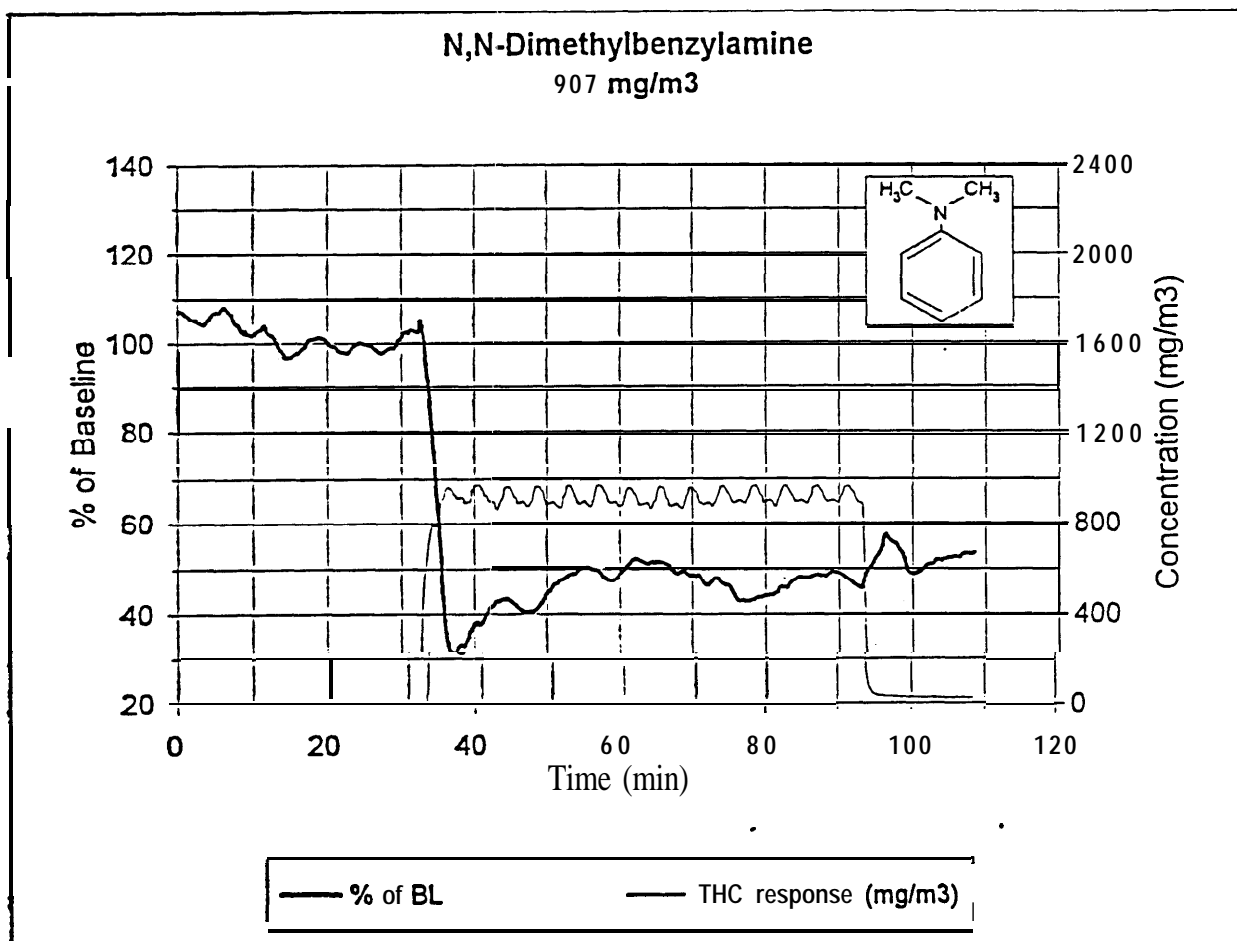


FIGURE B-25

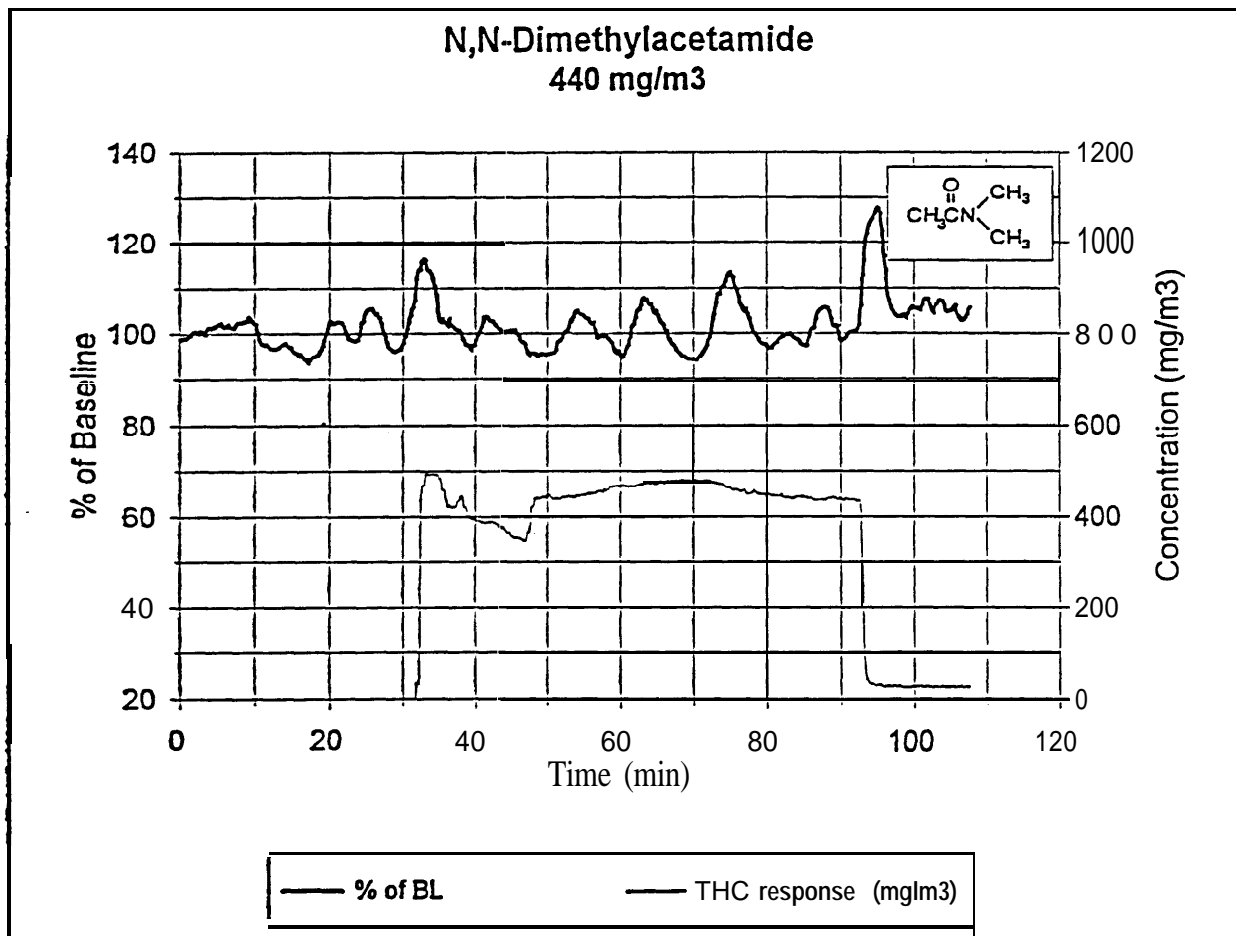


FIGURE B-27

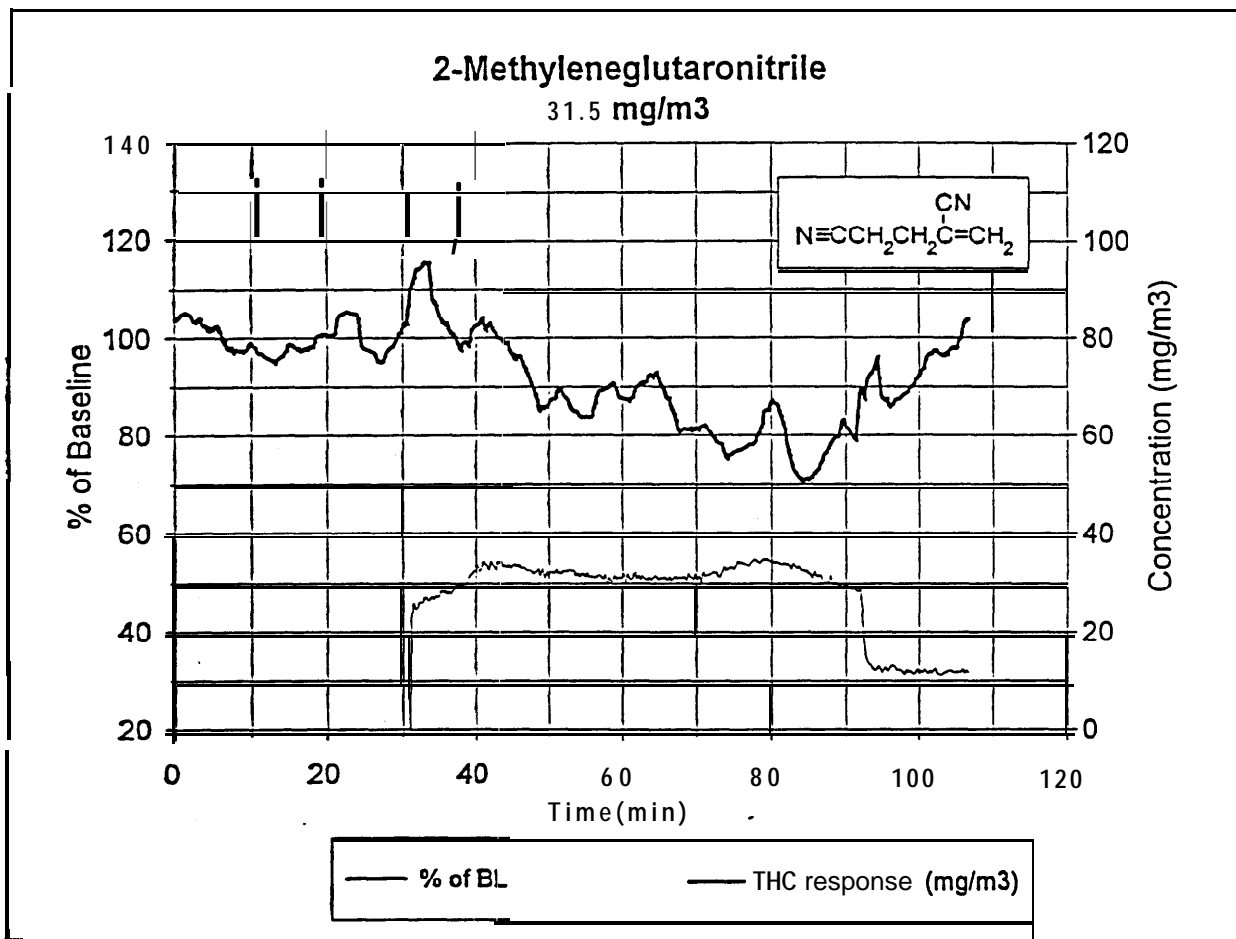


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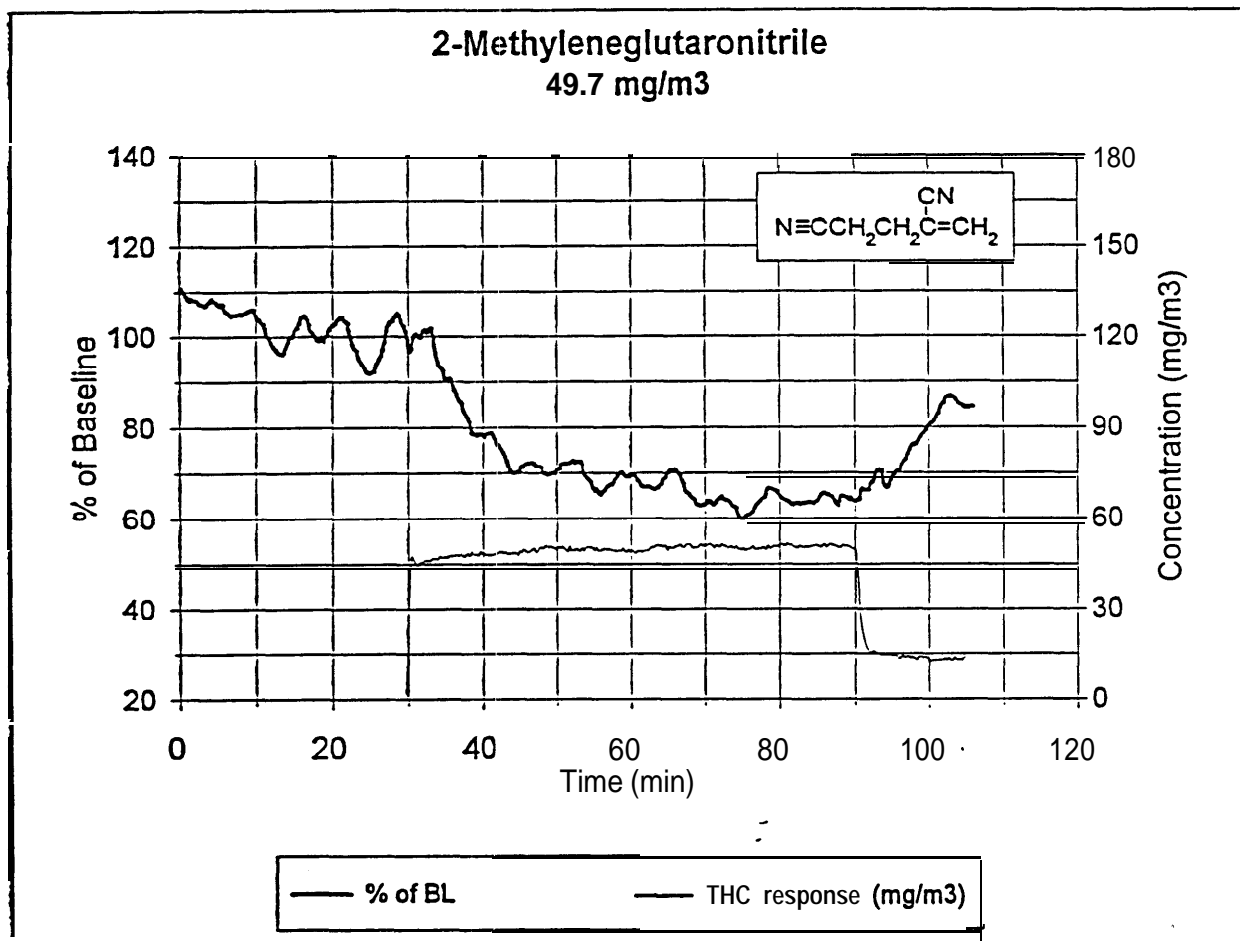


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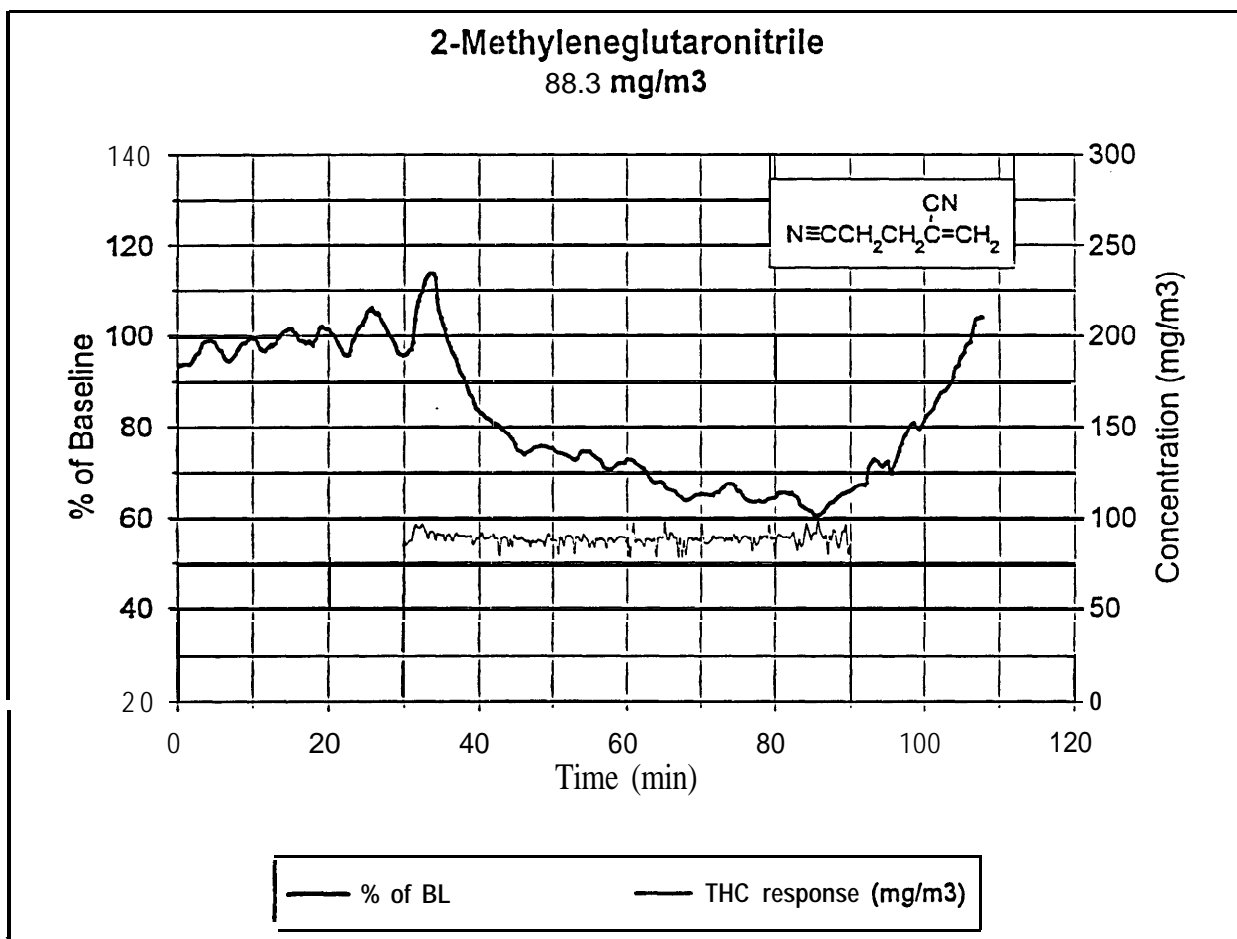


FIGURE B-40

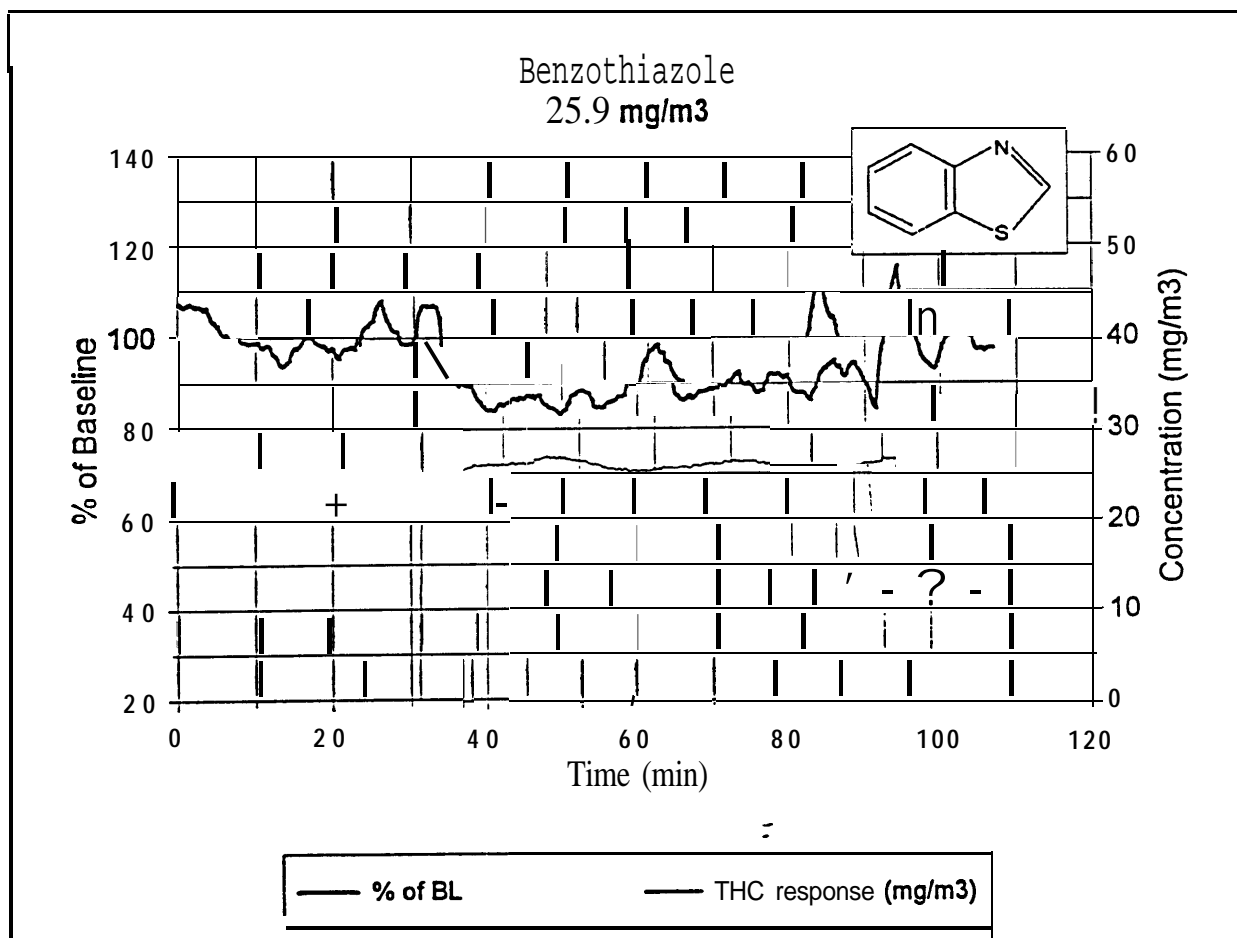


FIGURE B-41

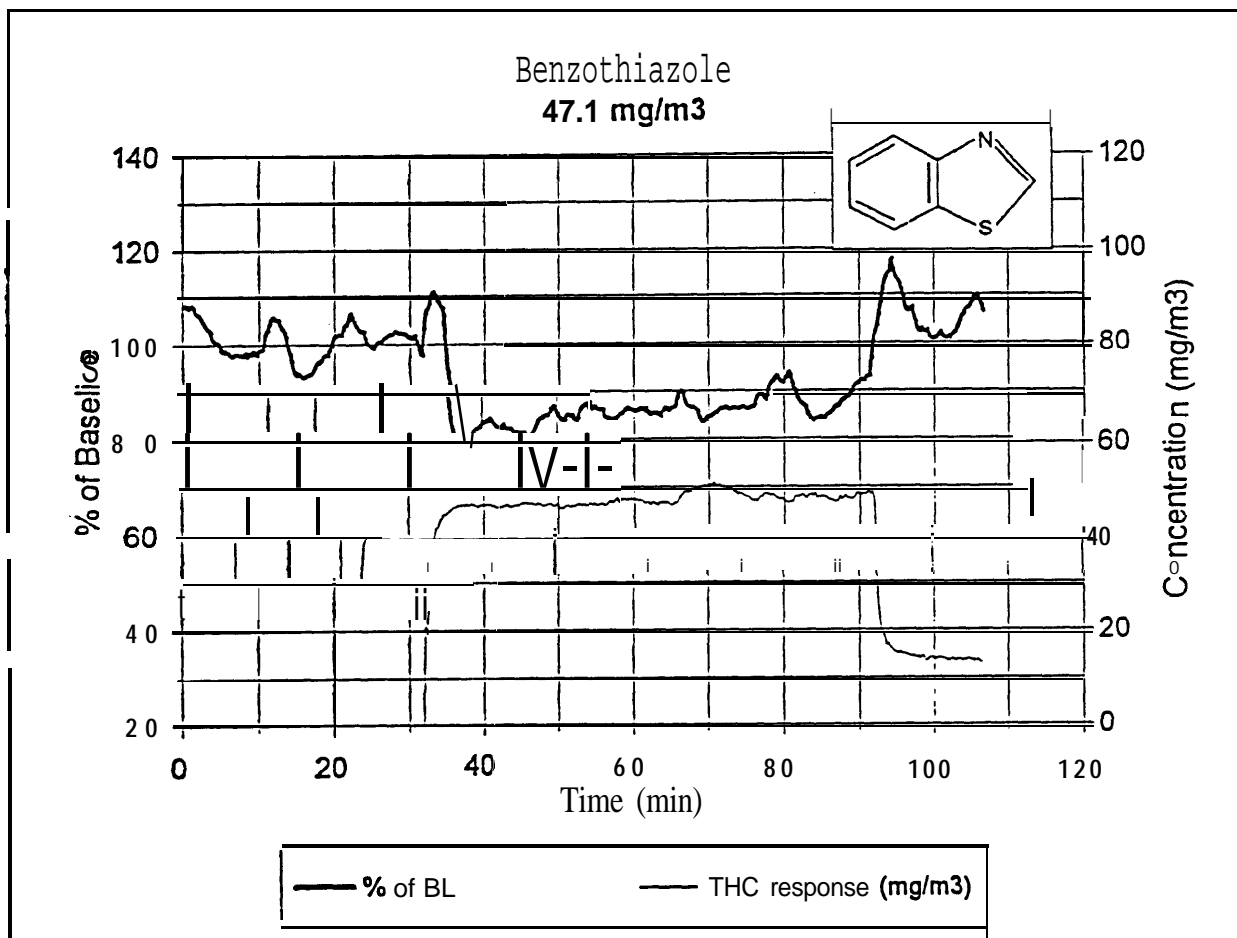


FIGURE B-42

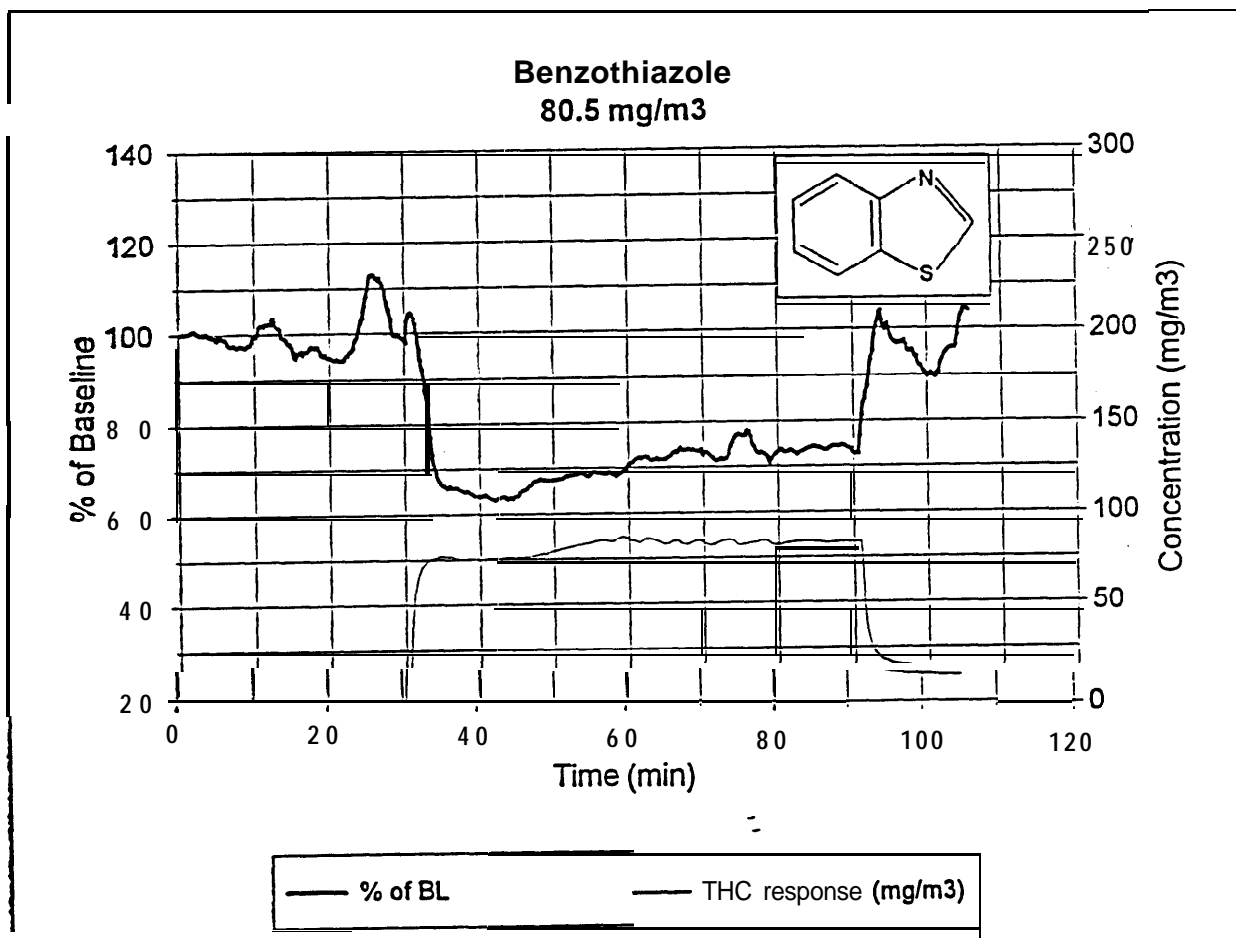


FIGURE B-43

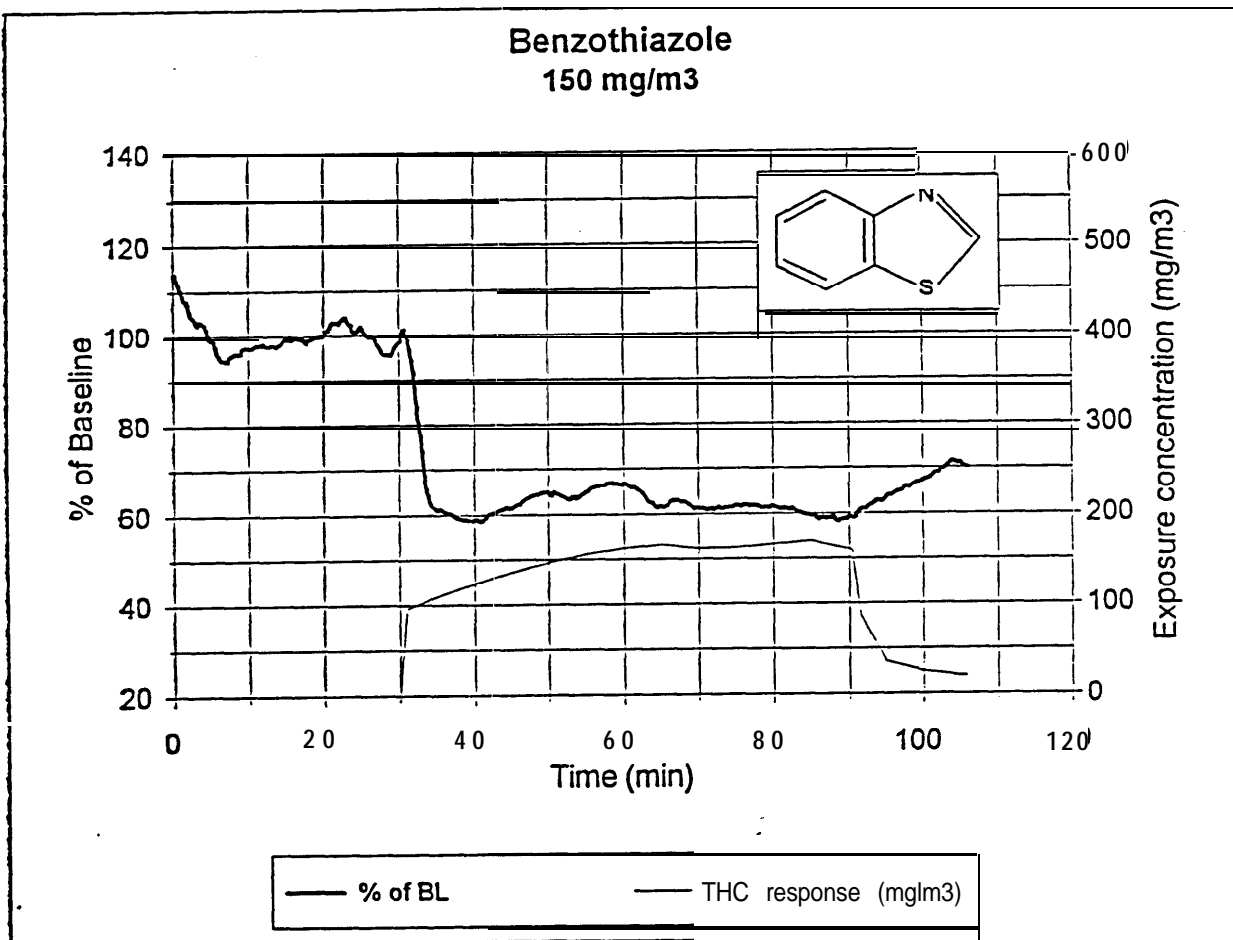


FIGURE B-44

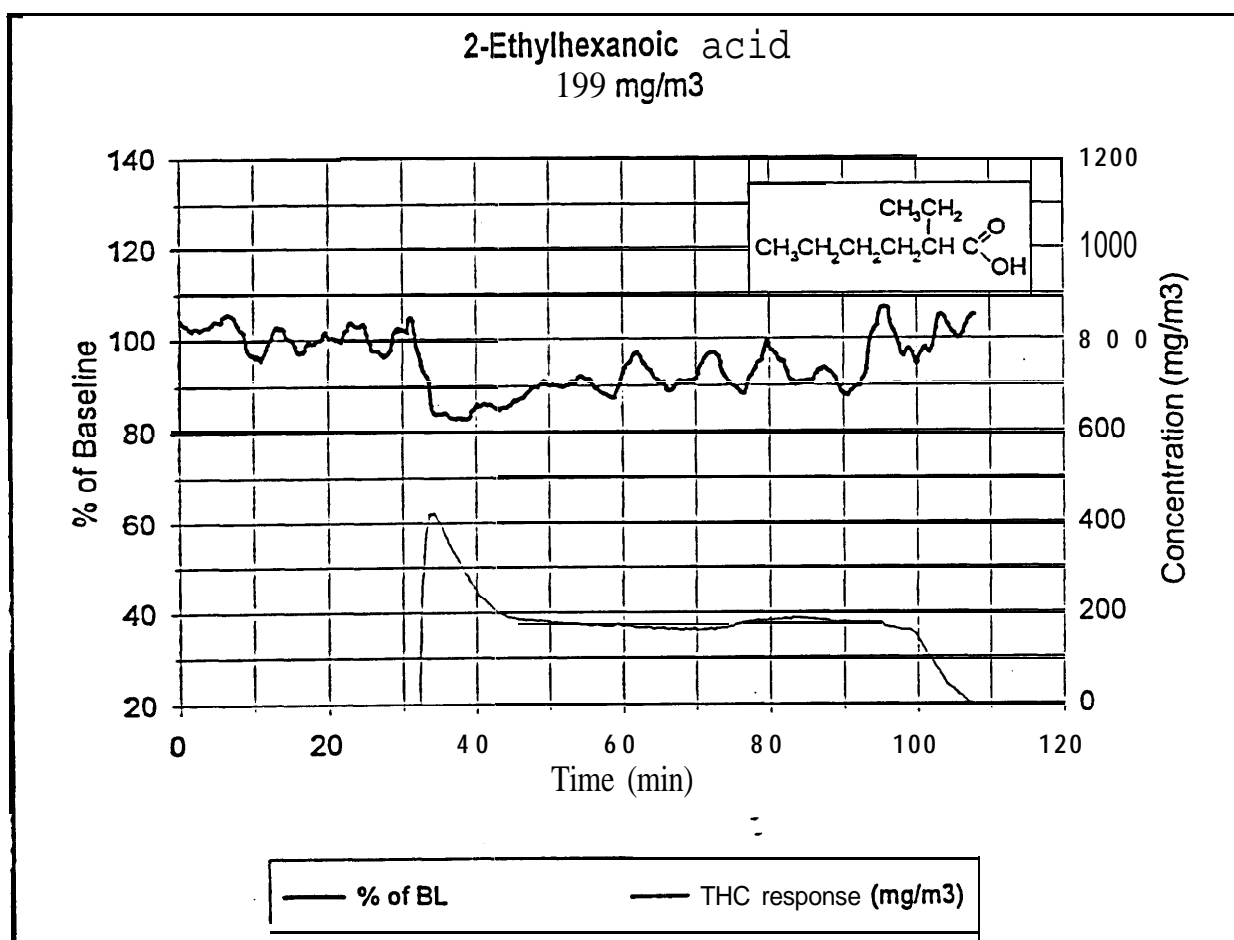


FIGURE B-45

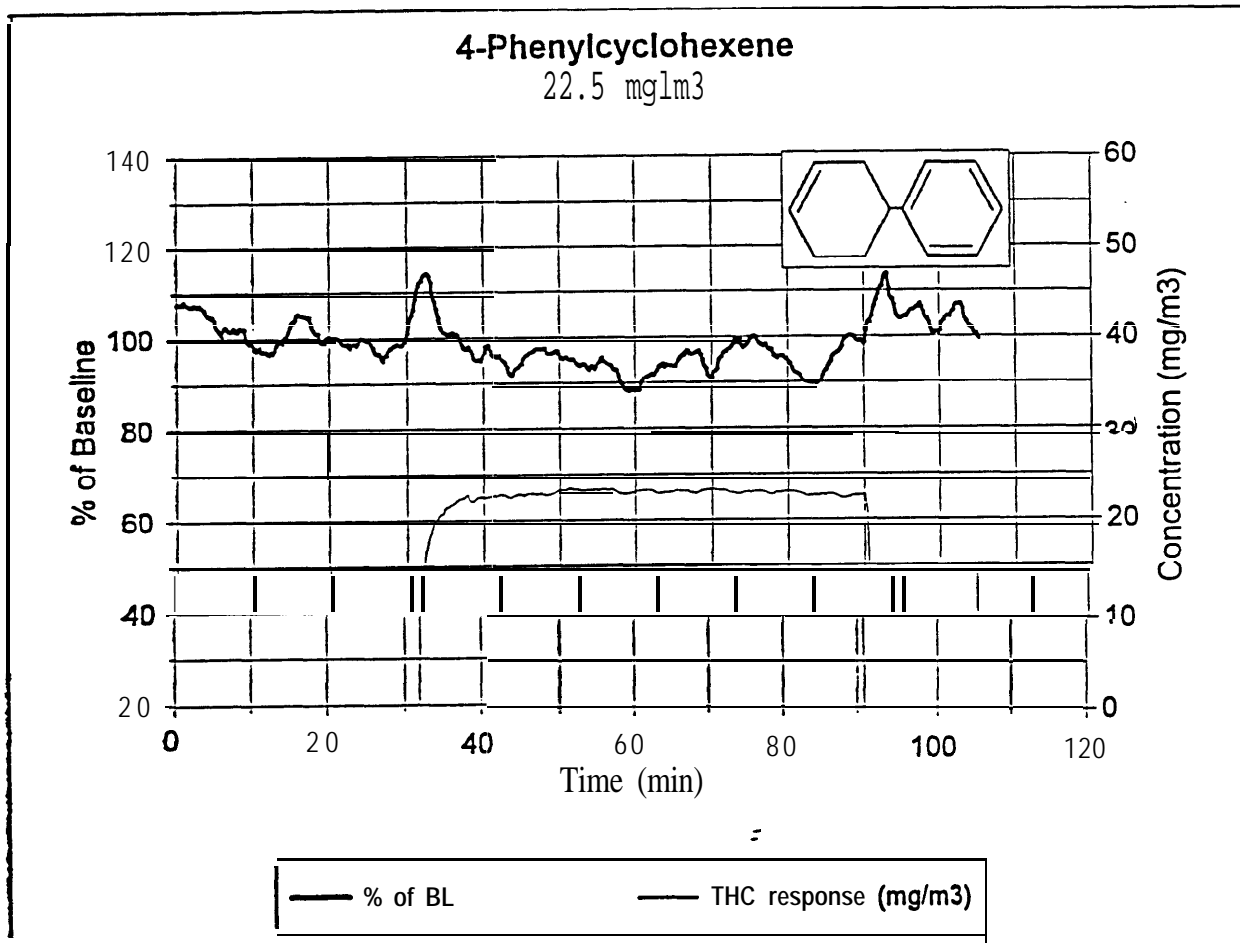


FIGURE B-46

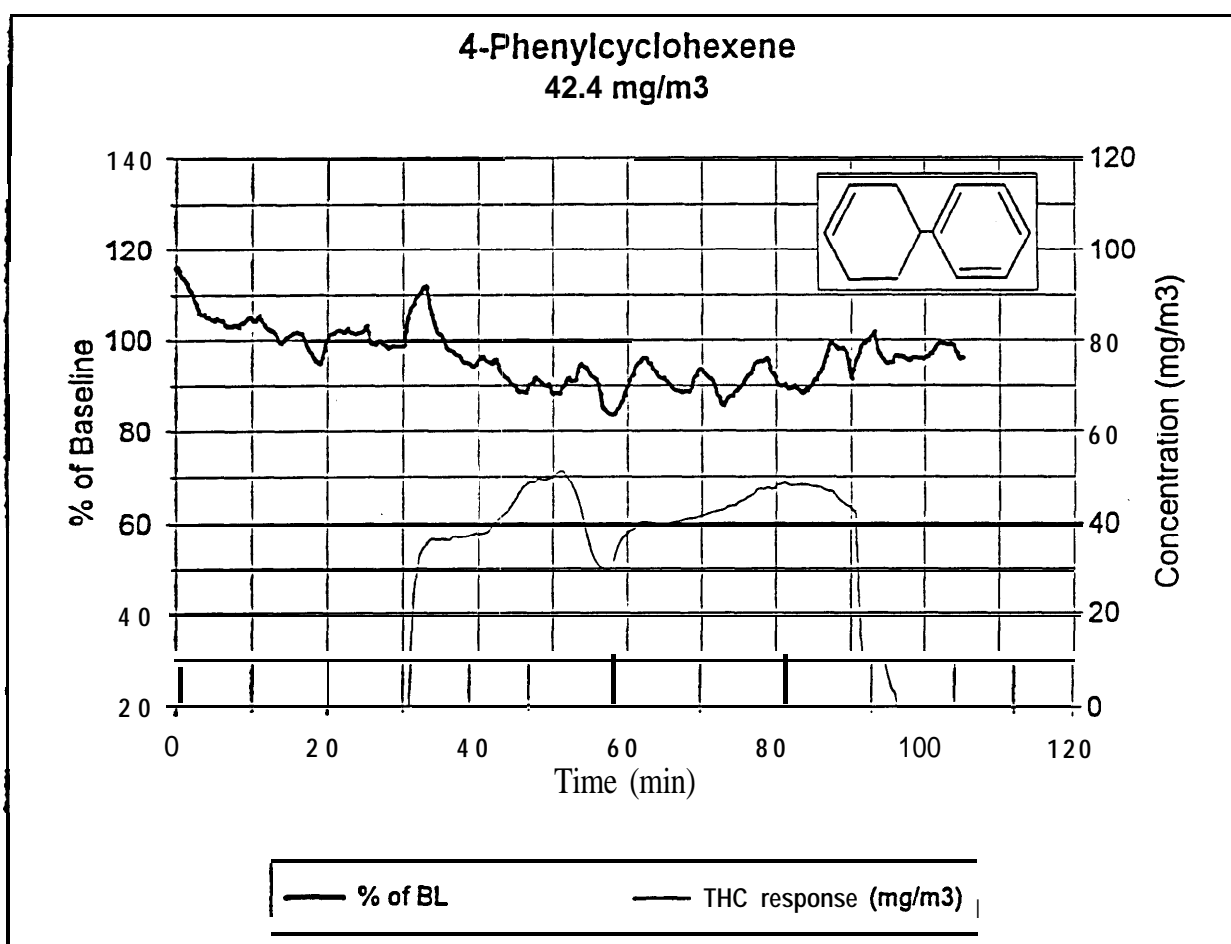


FIGURE B-47

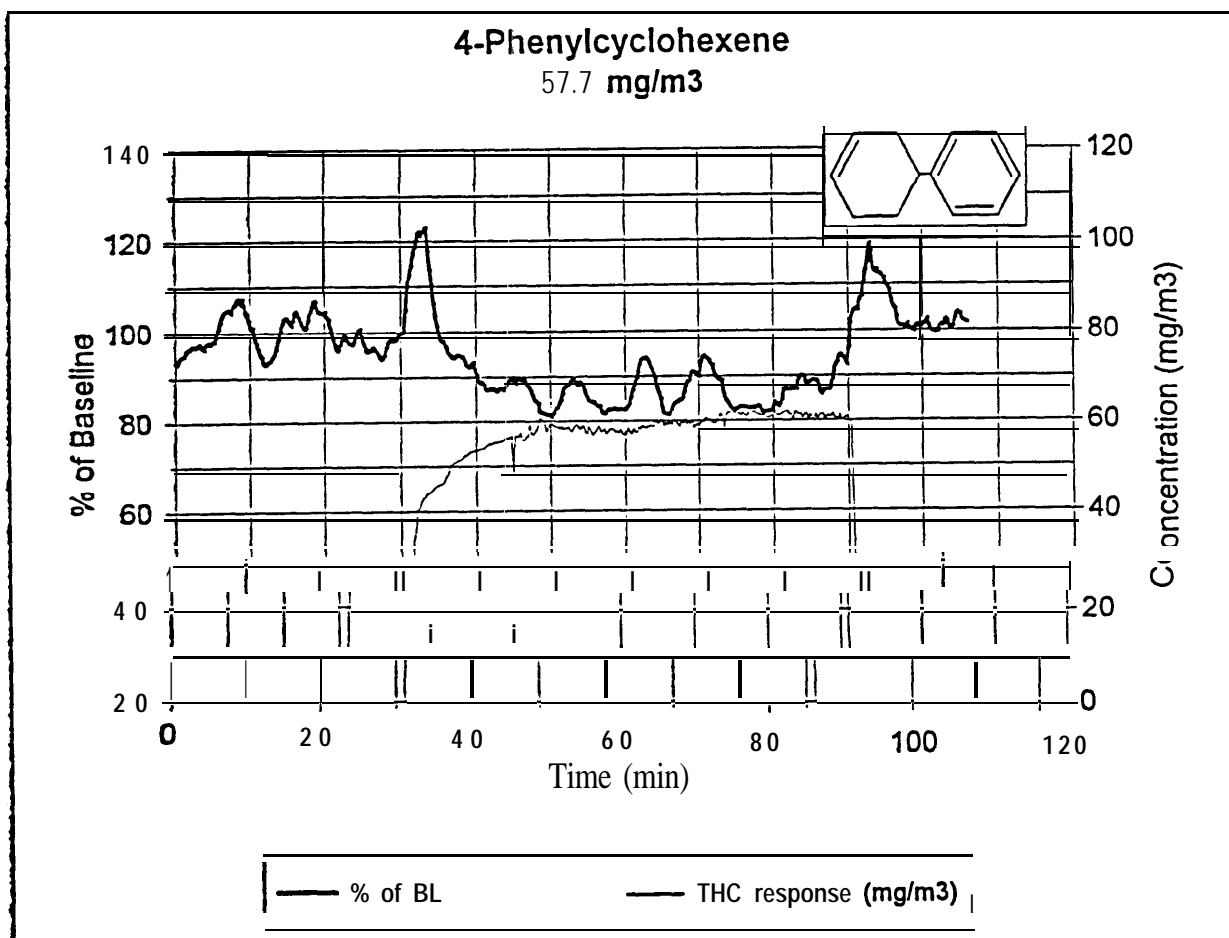


FIGURE B-48

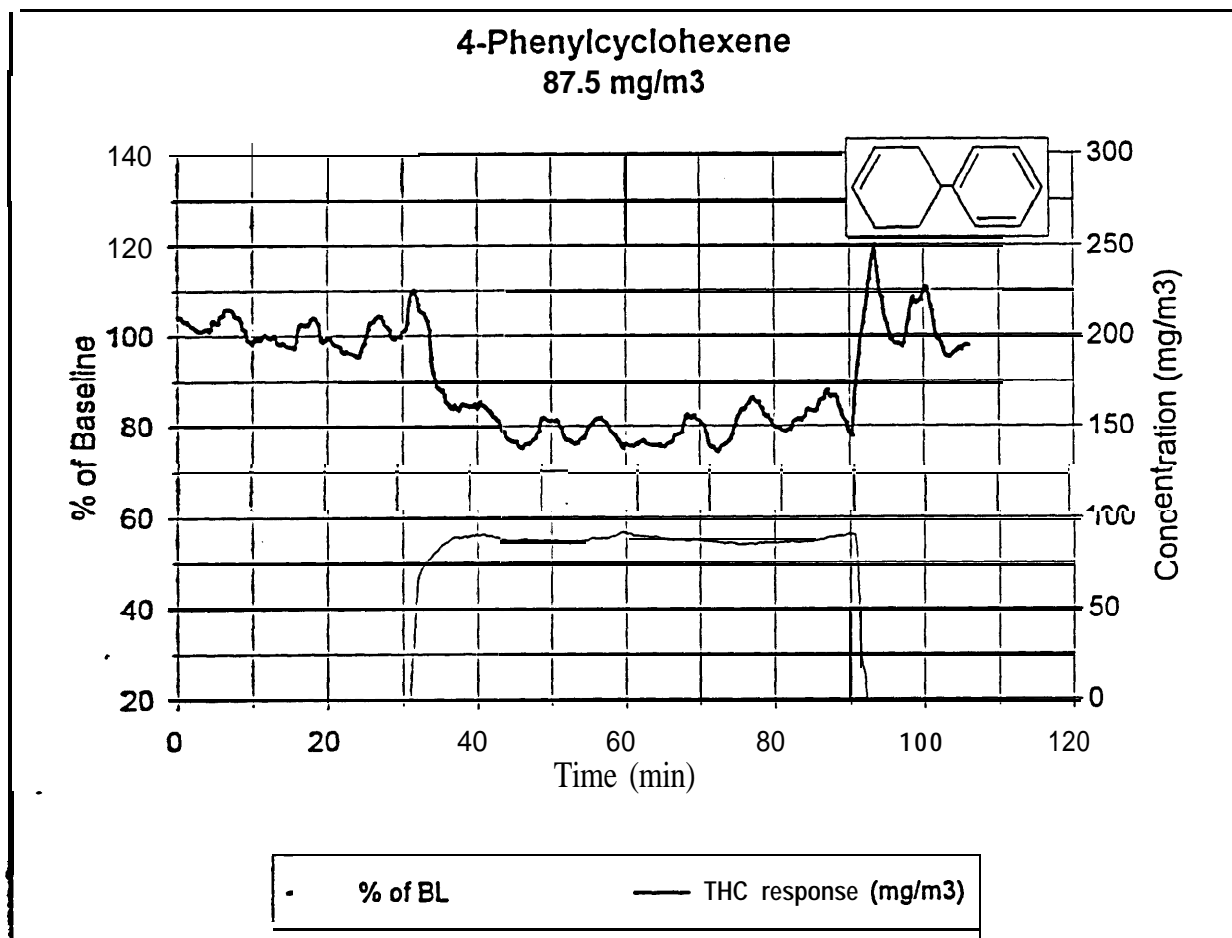


FIGURE B-49

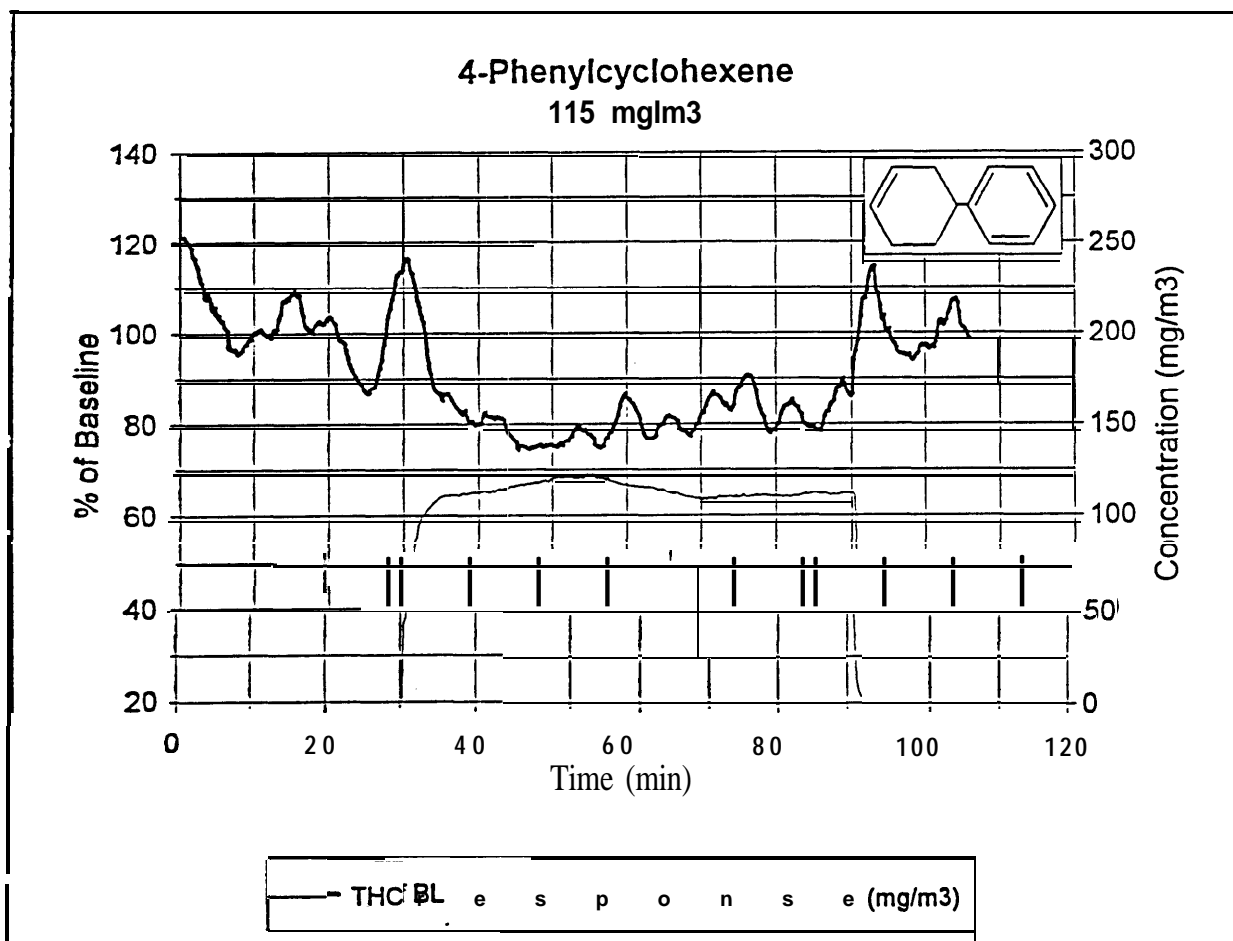


FIGURE B-50

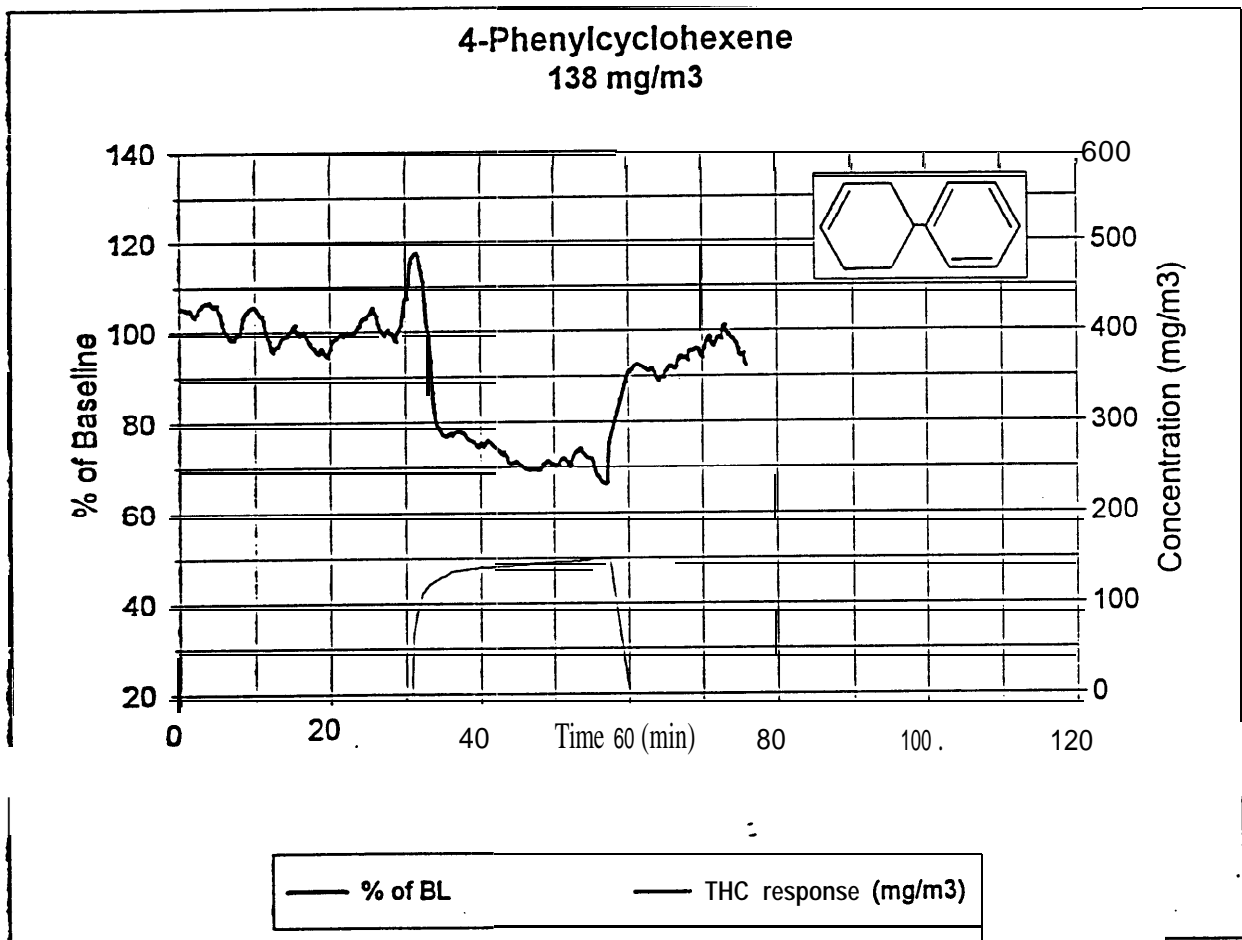


FIGURE B-51

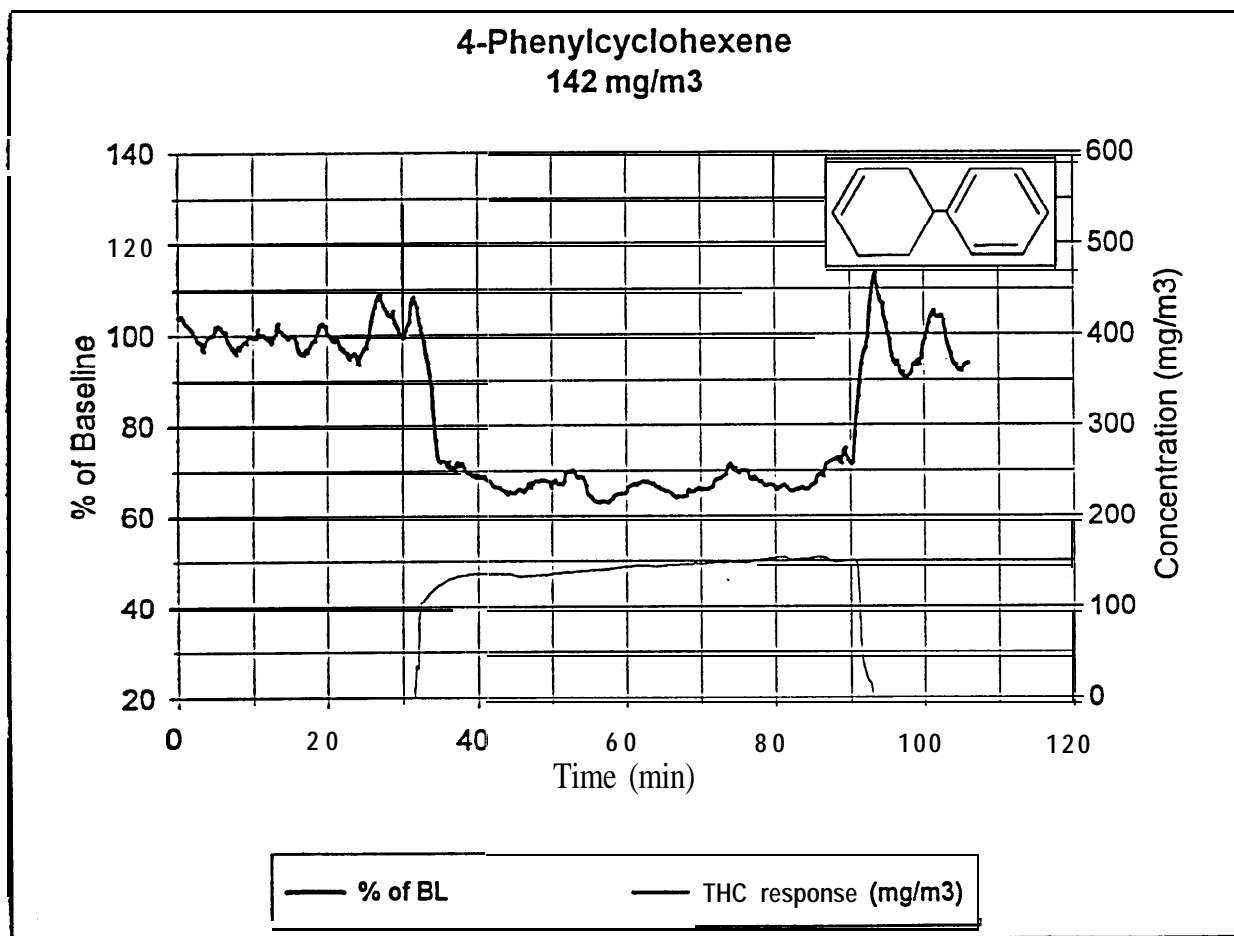


FIGURE B-52

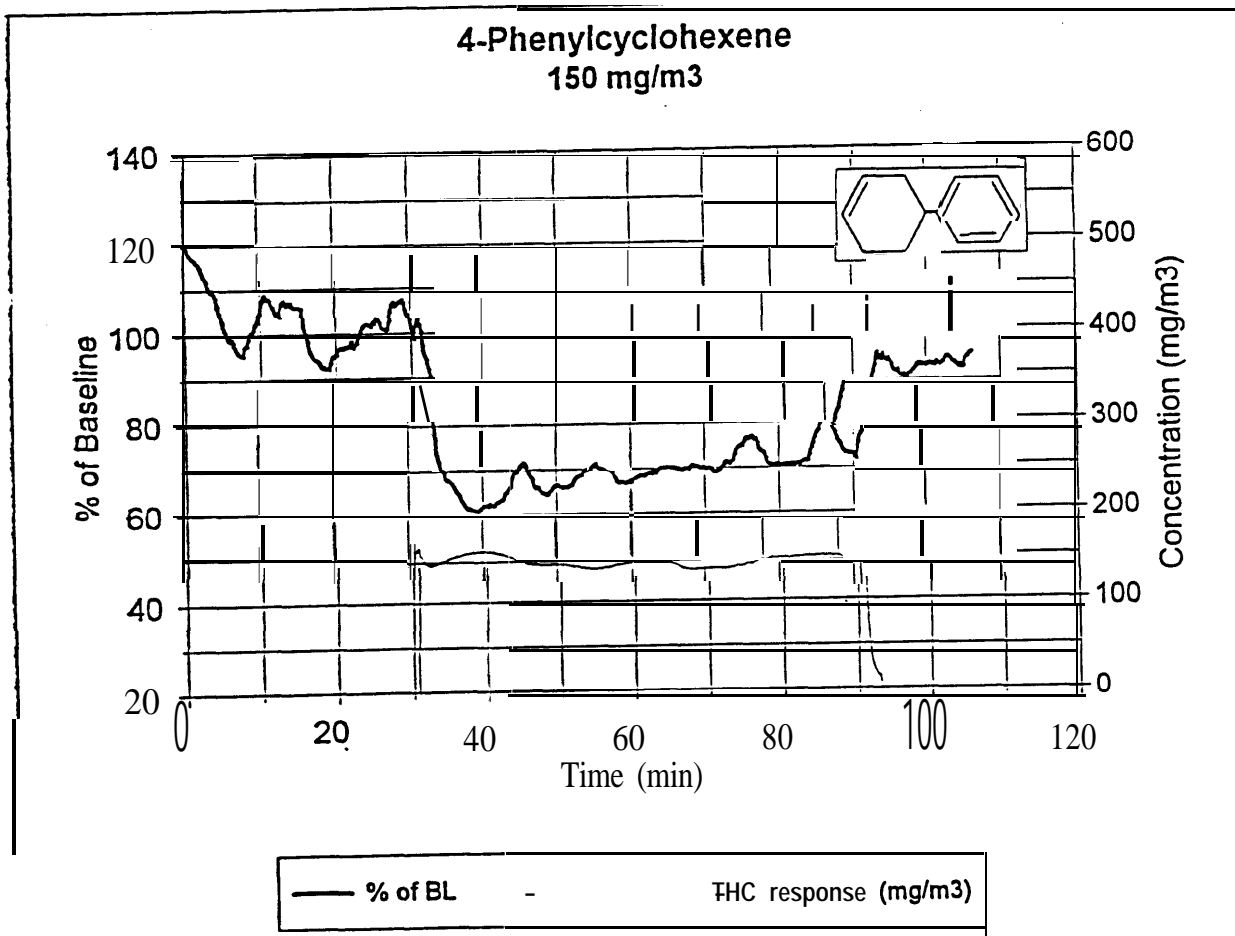


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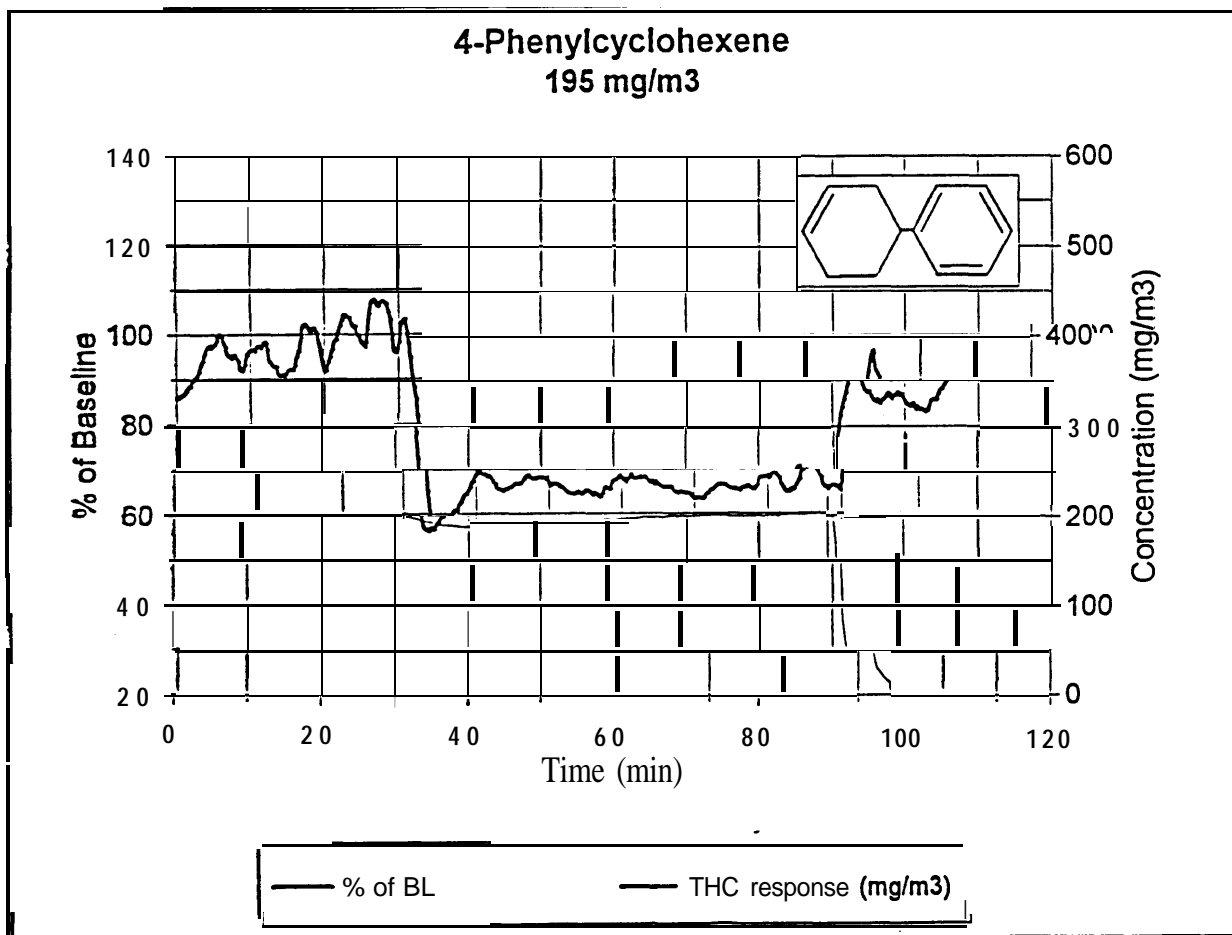


FIGURE B-54

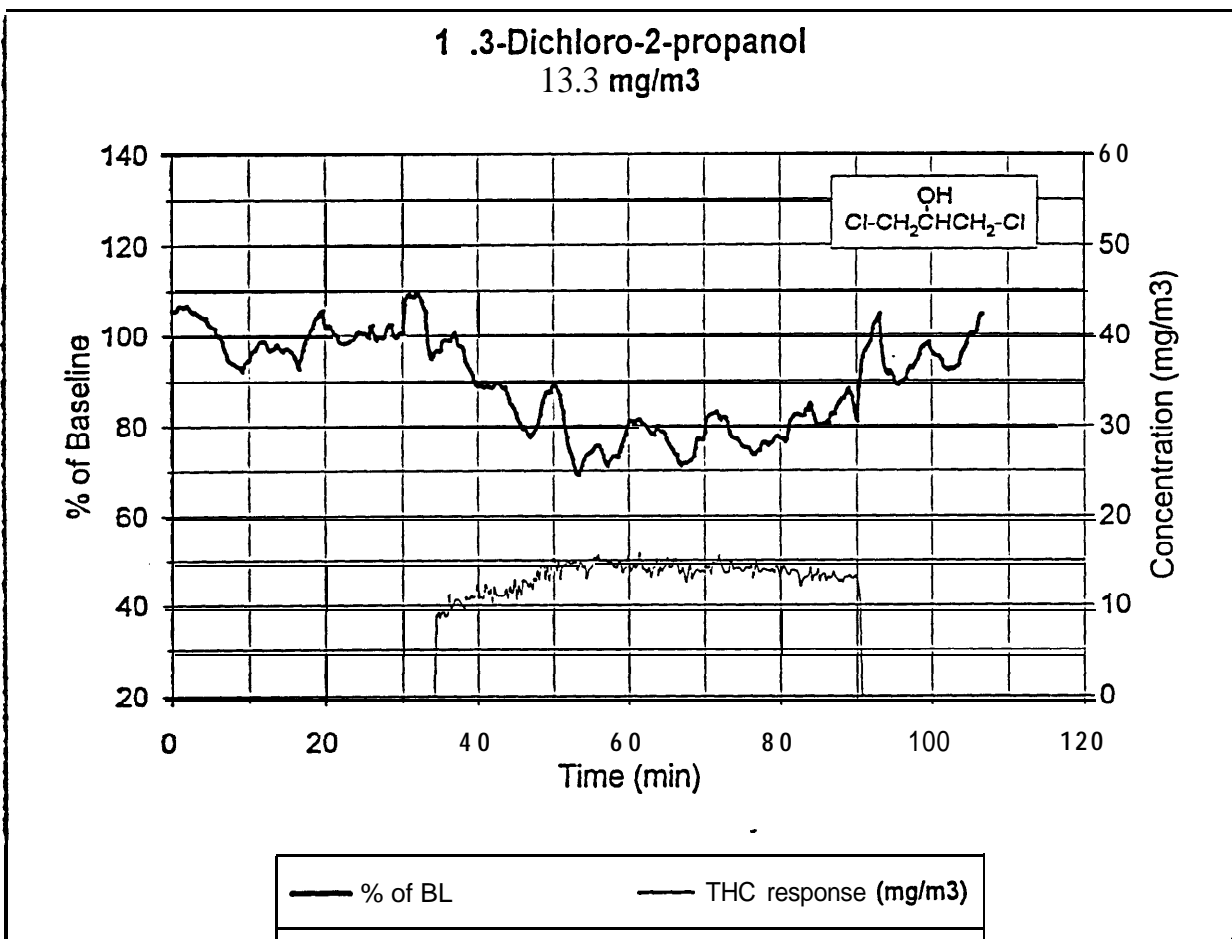


FIGURE B-55

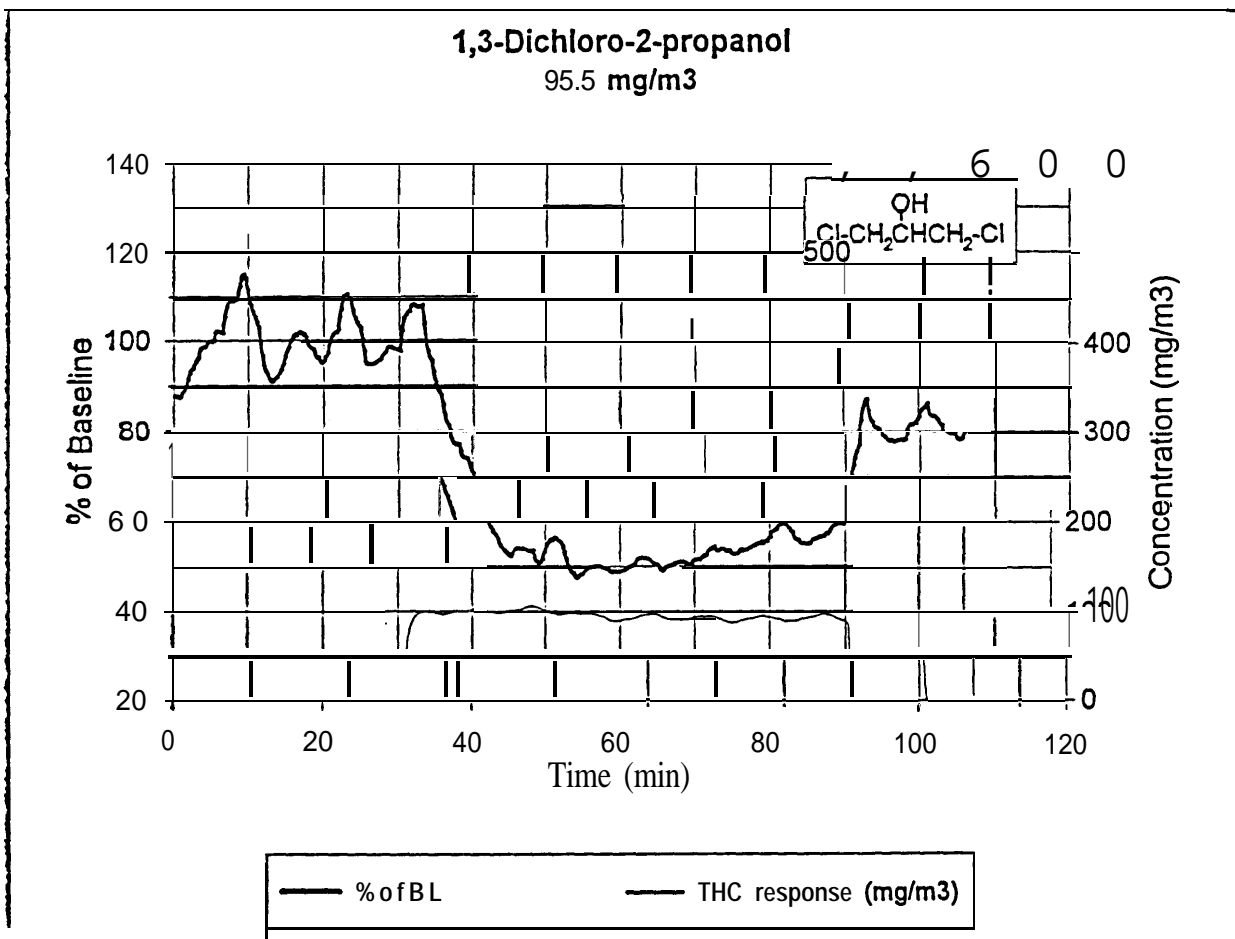


FIGURE B-56

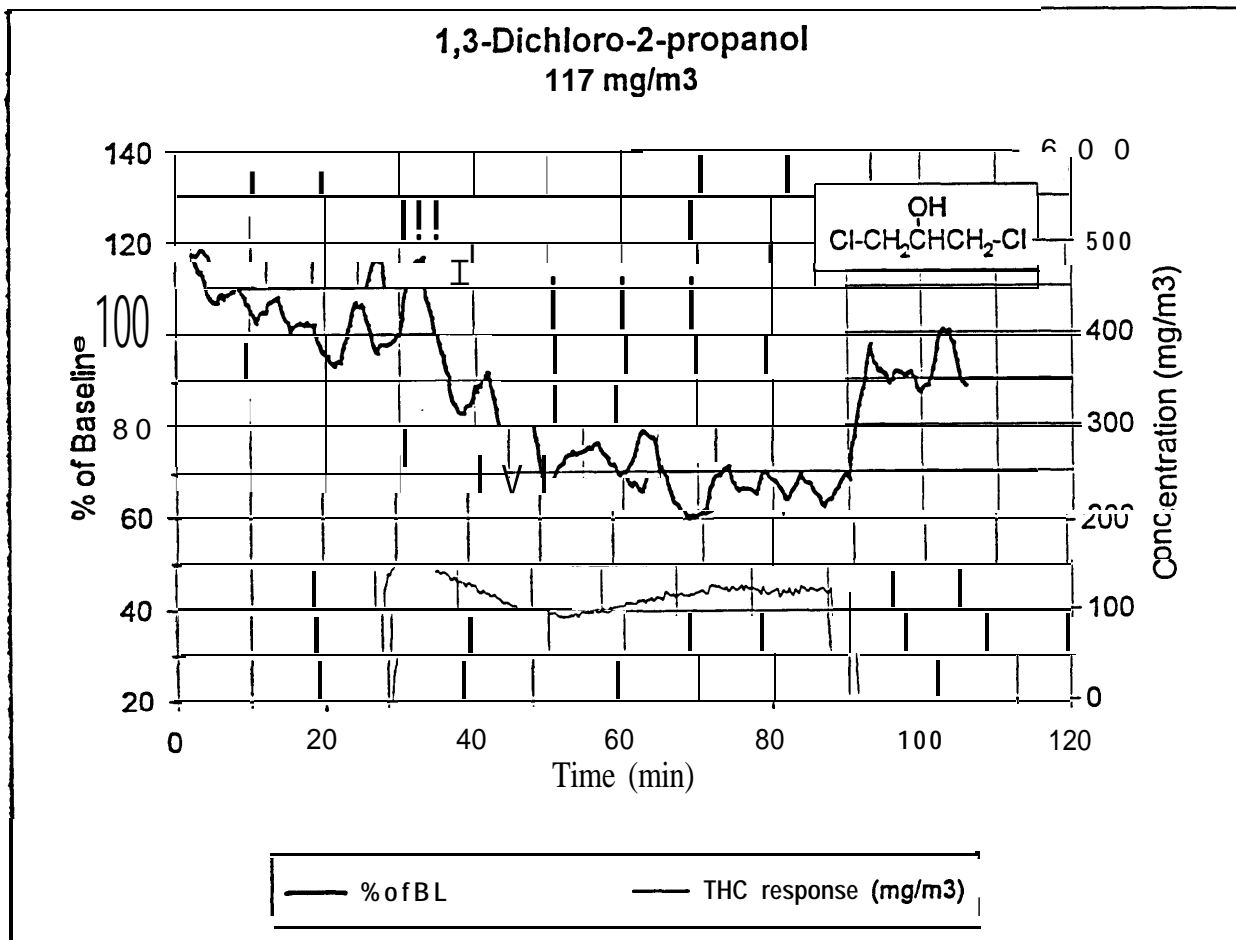


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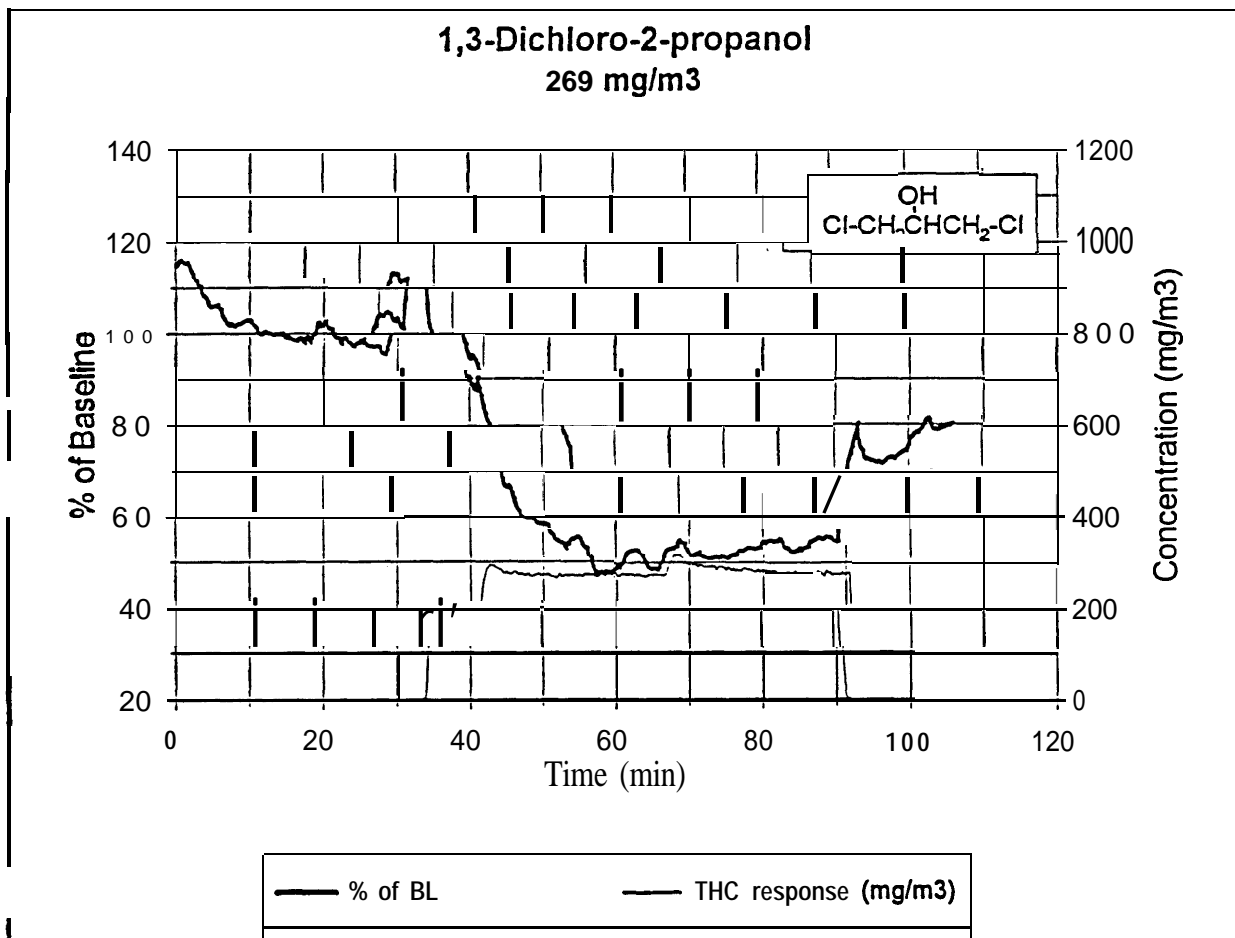


FIGURE B-58

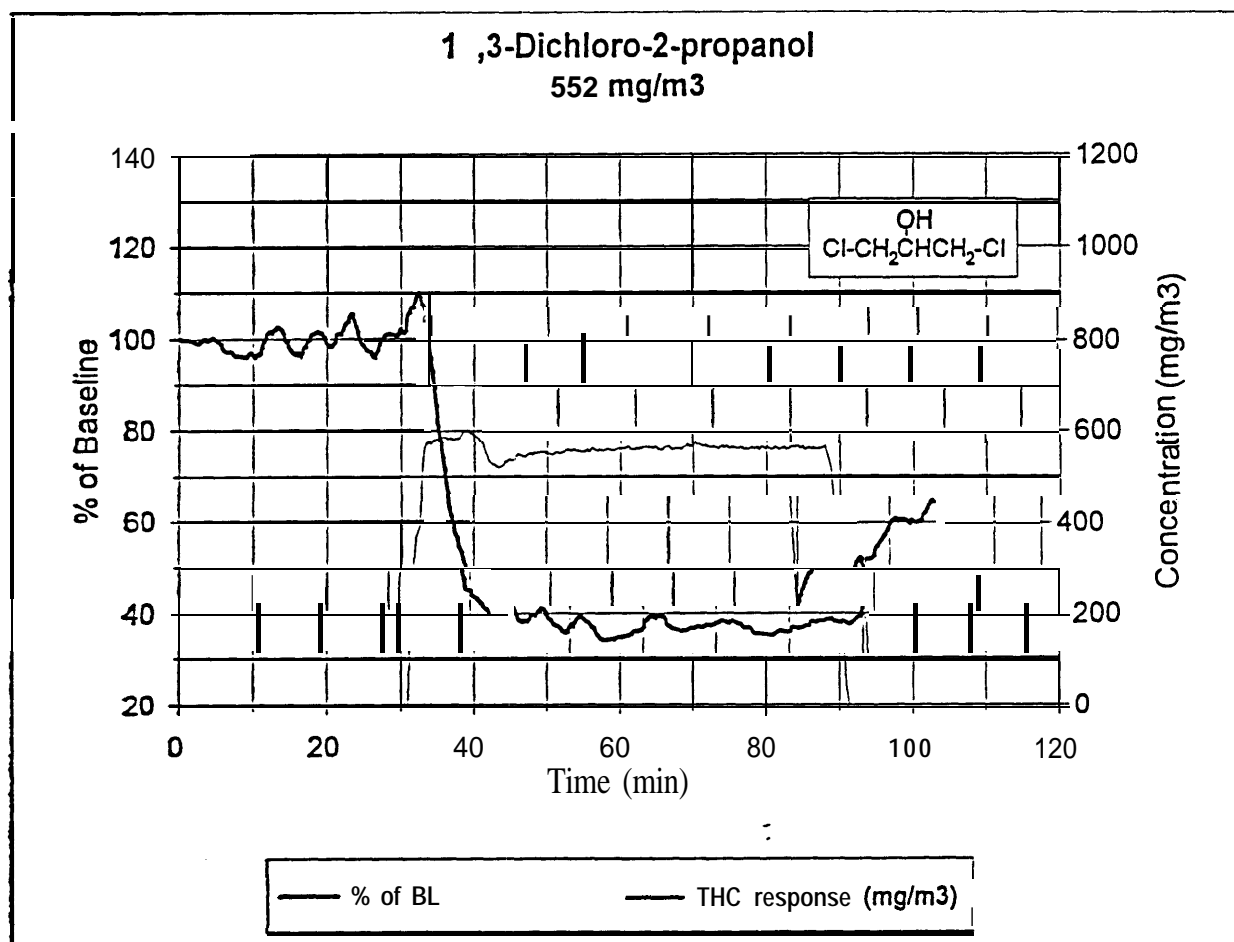


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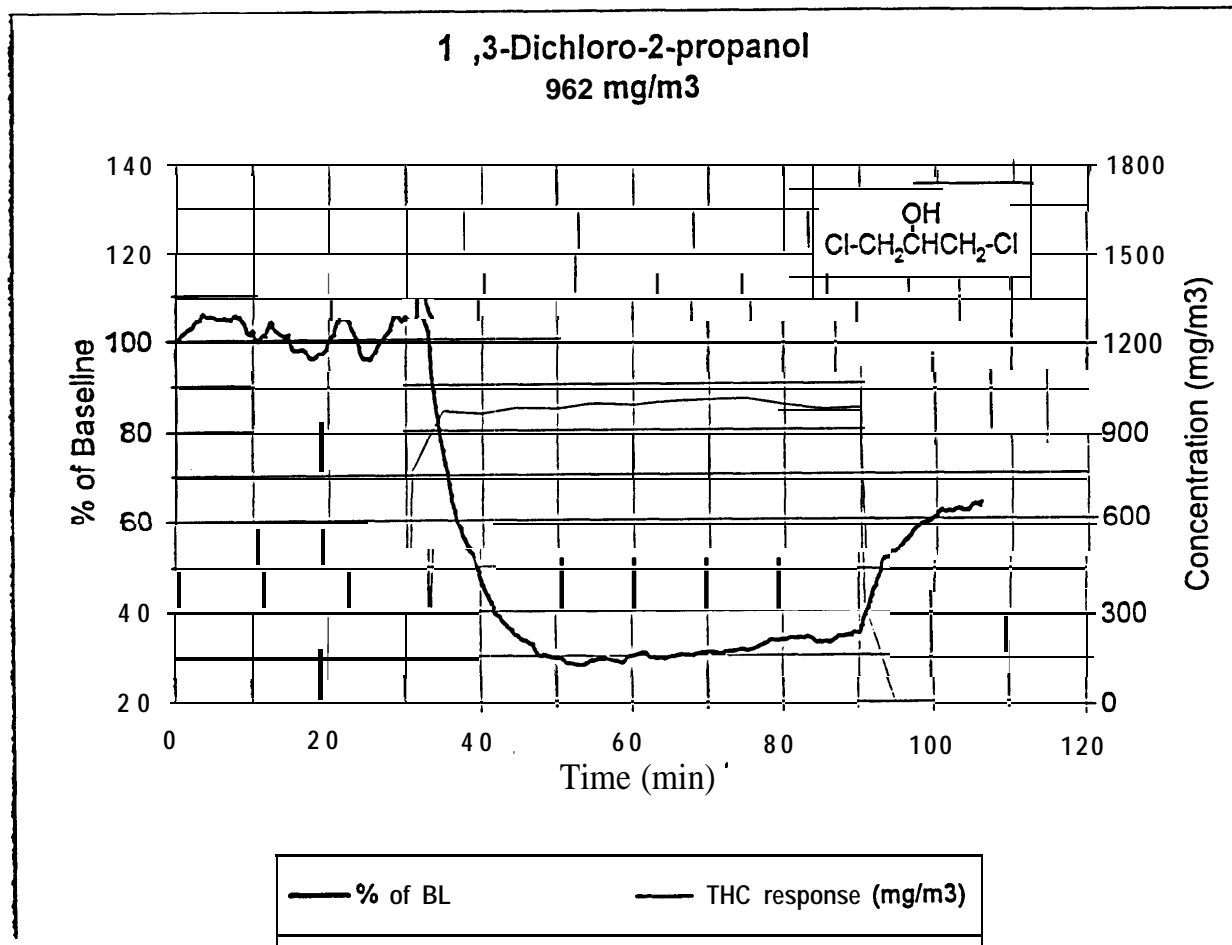


FIGURE B-60

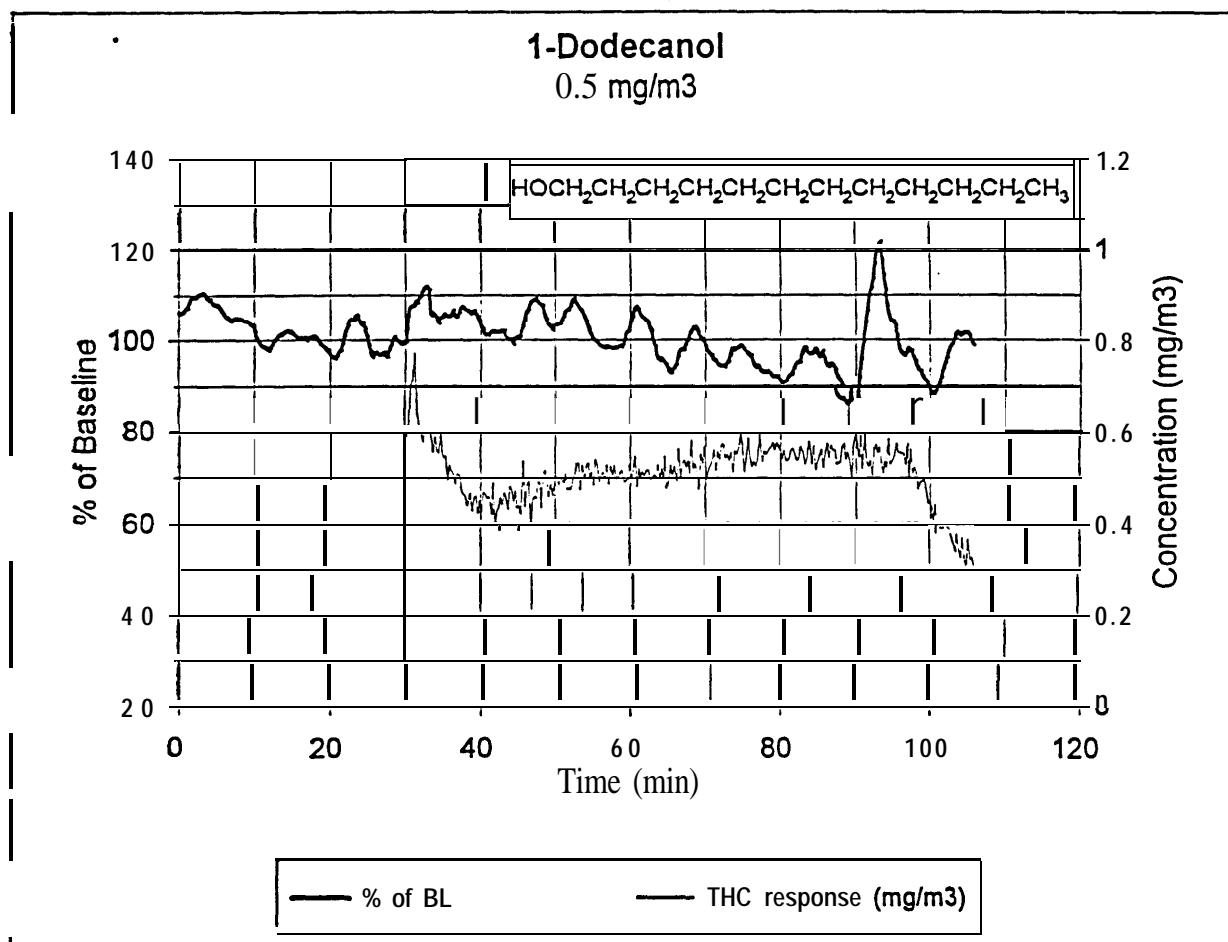


FIGURE B-61

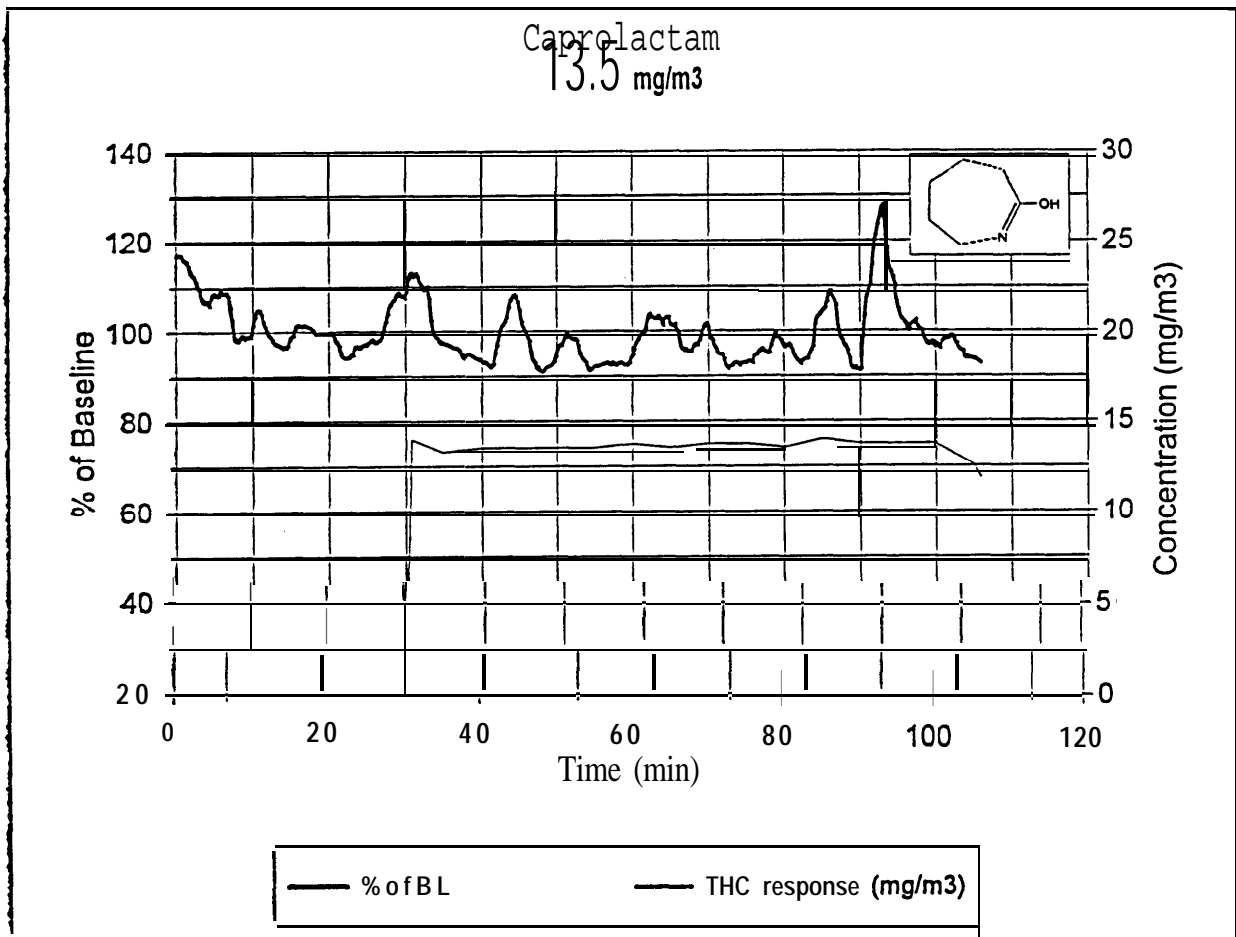


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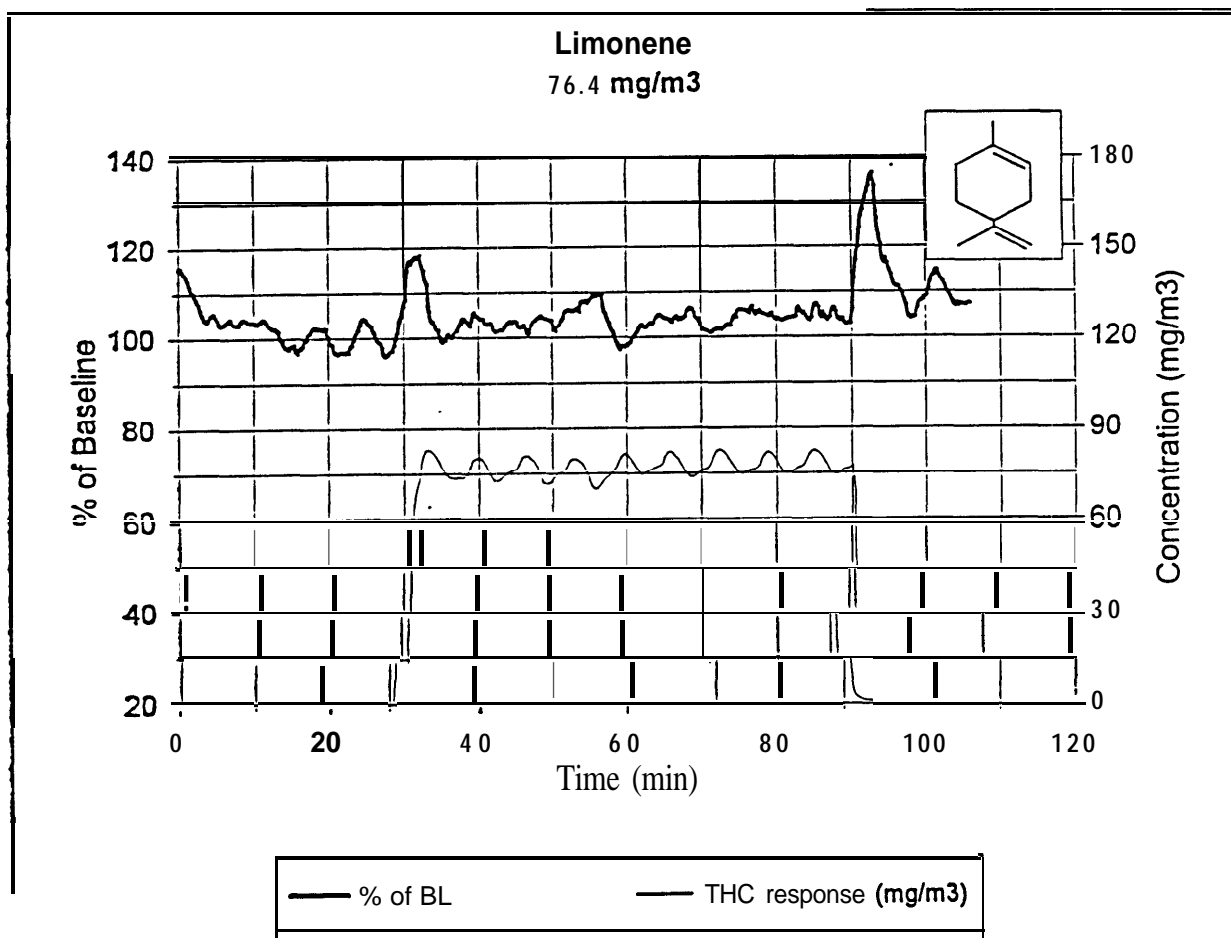


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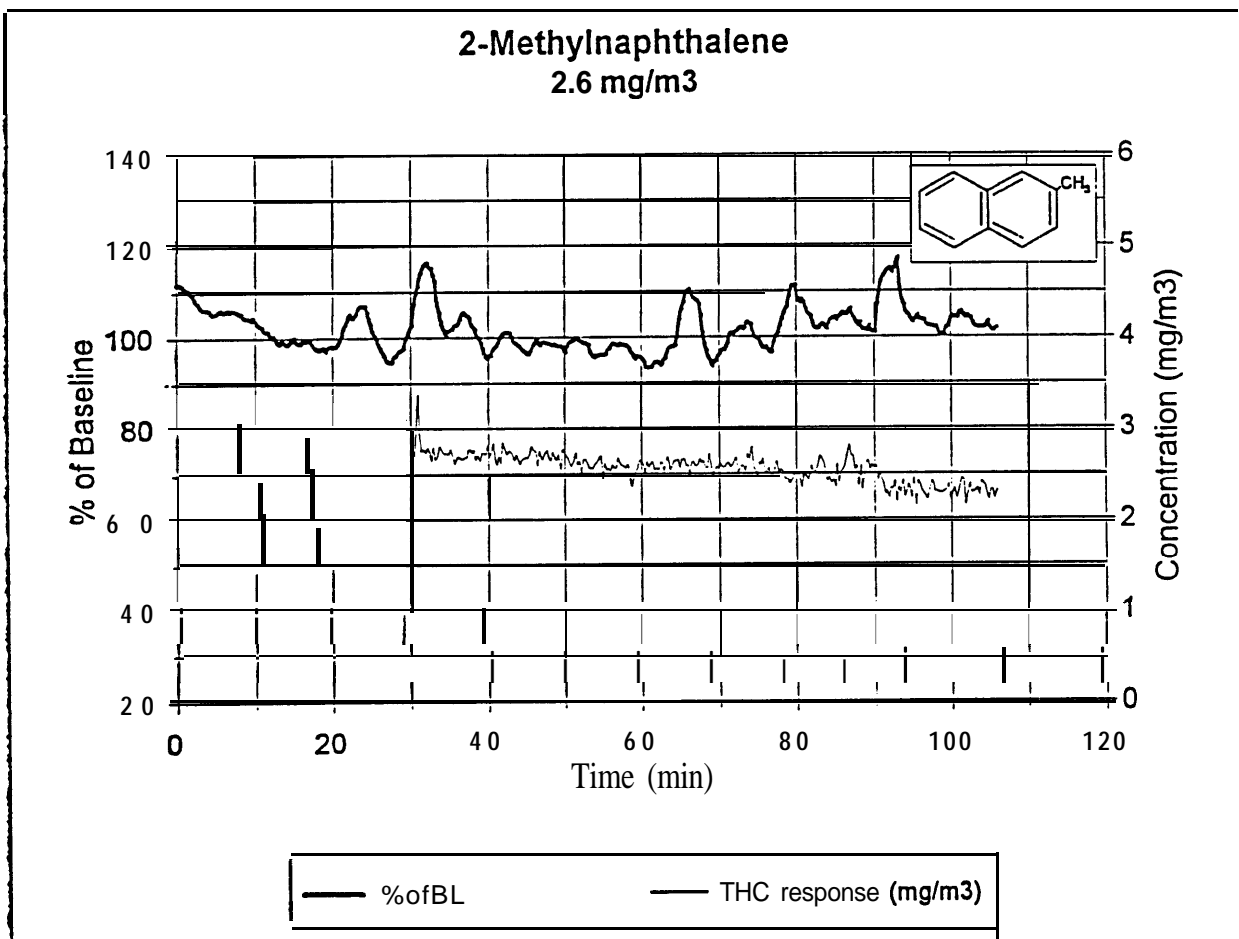


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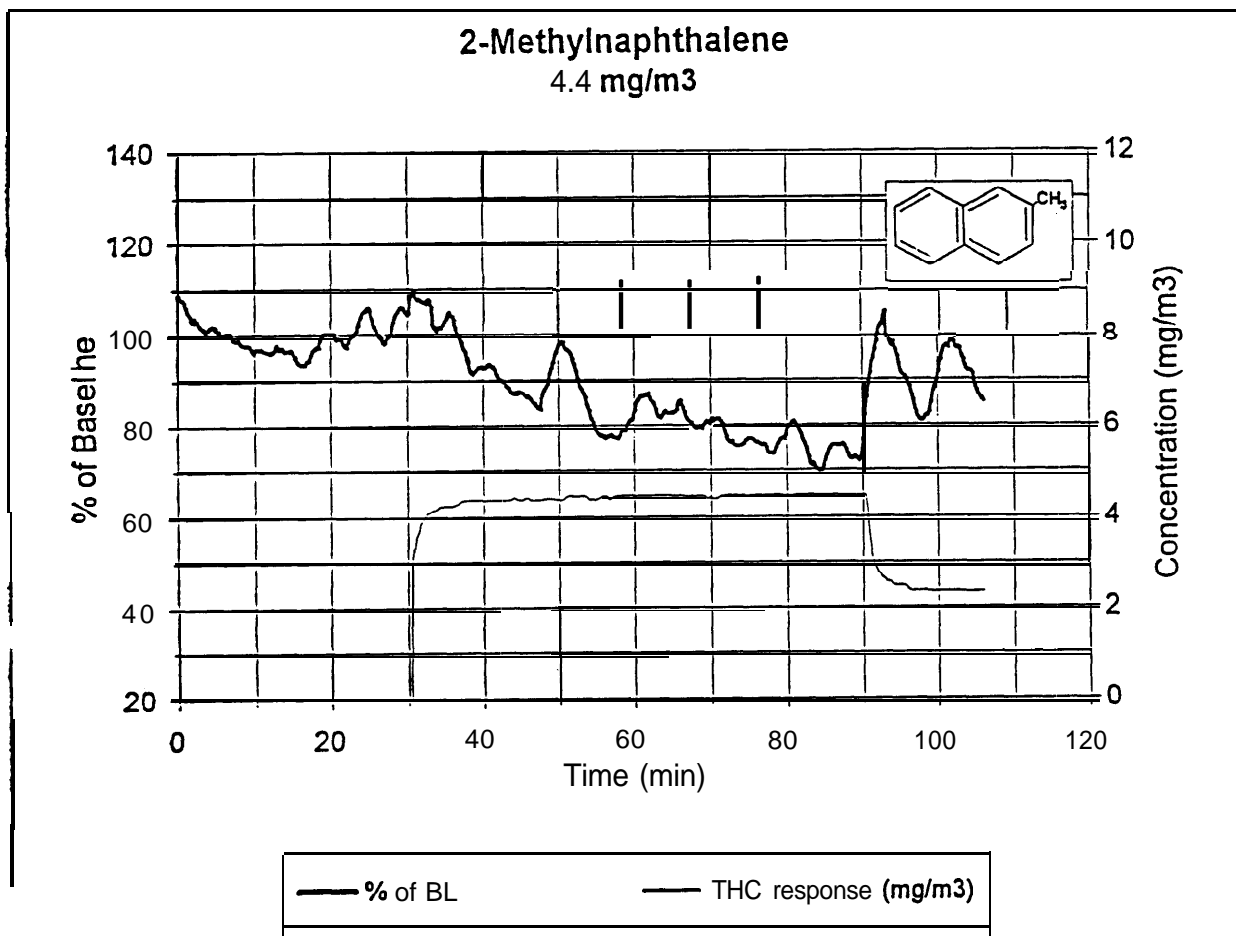


FIGURE B-65

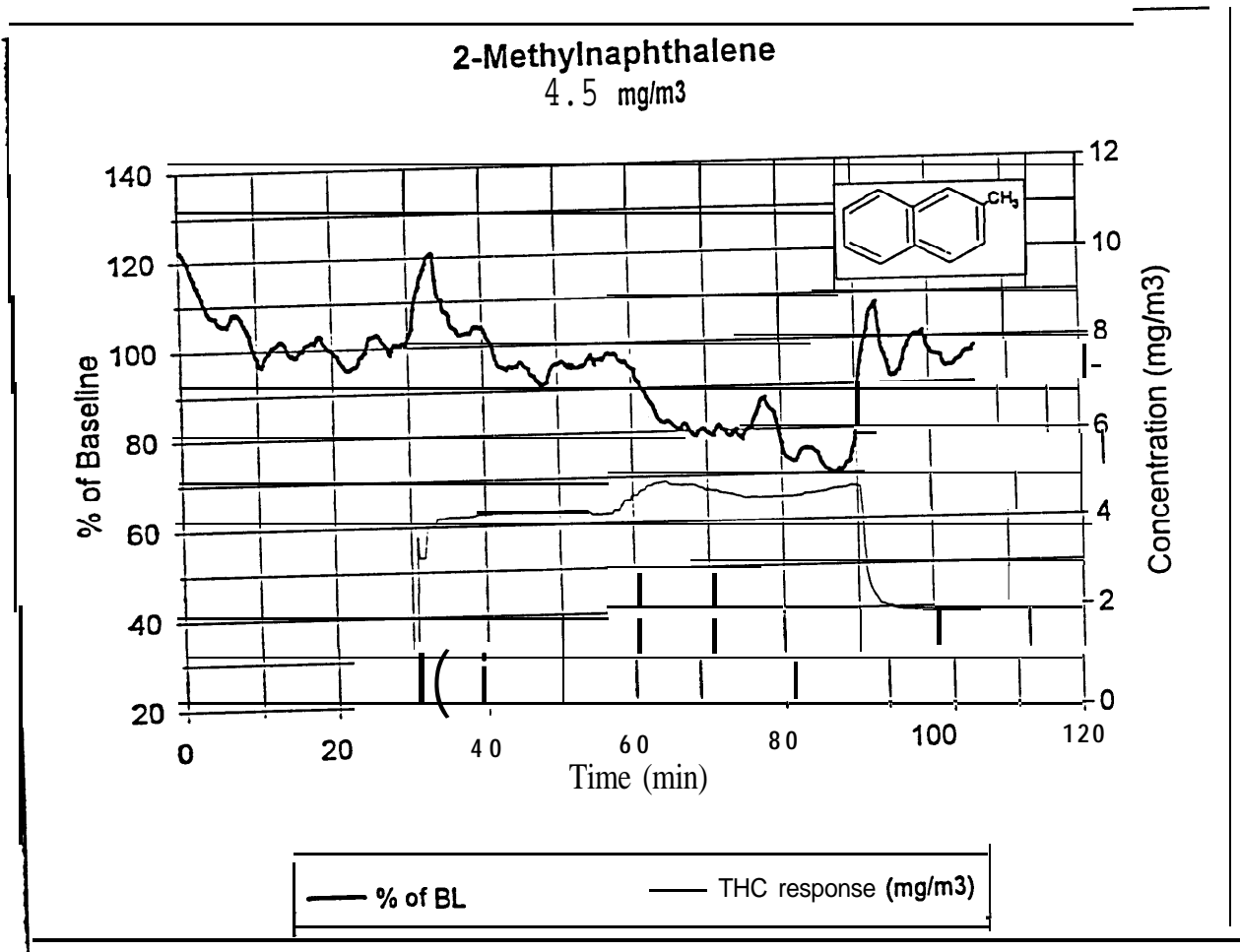


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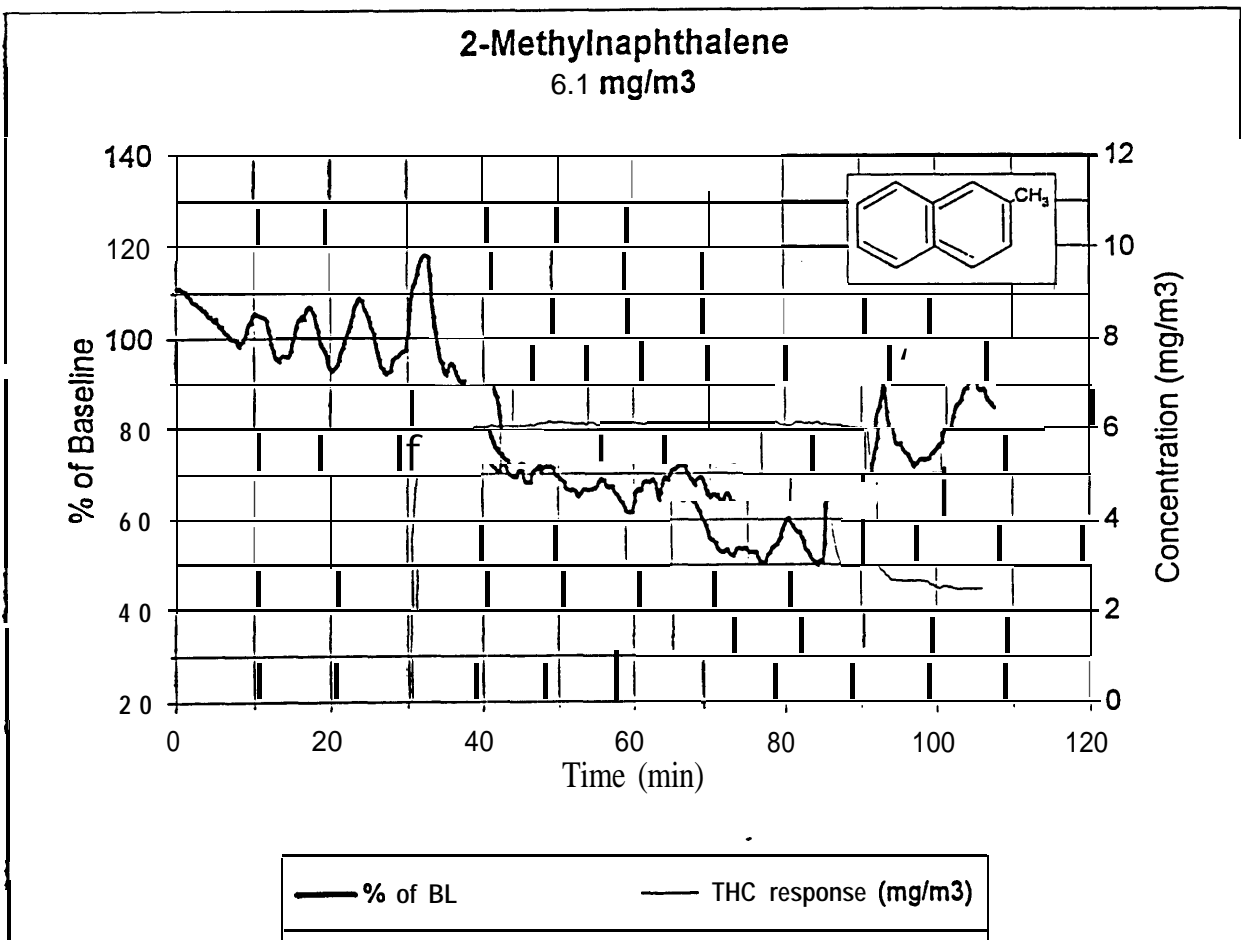


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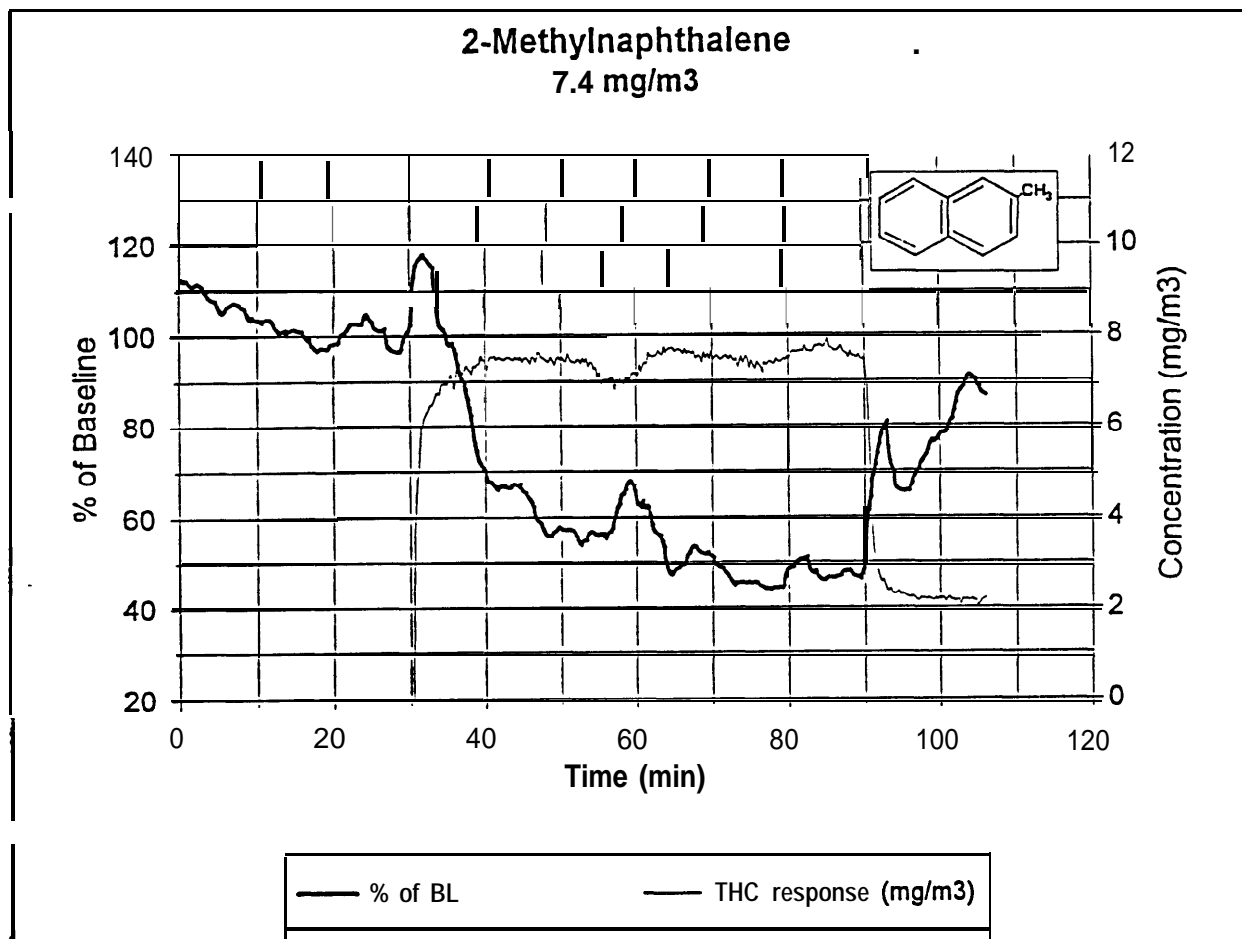


FIGURE B-68

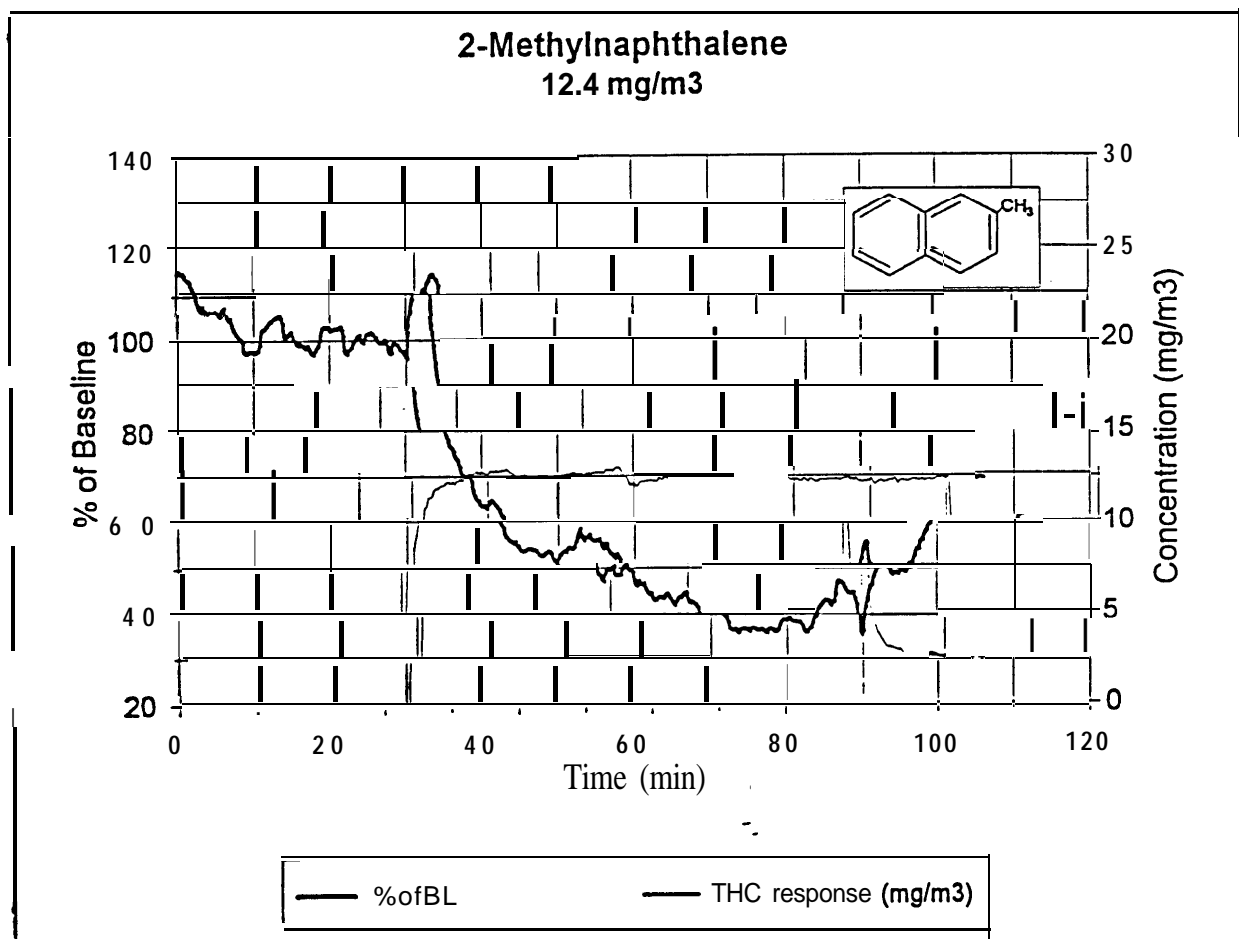


FIGURE B-69

