

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE

MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

NAPHTHALENE

SB 950 # 080, Tolerance # 50232

October 29, 1986

Revised 5/22/87, 11/22/88, 8/8/89

I. DATA GAP STATUS

Chronic toxicity, rat:	Data gap, no study on file
Chronic toxicity, dog:	Data gap, no study on file
Oncogenicity, rat:	Data gap, no study on file
Oncogenicity, mouse:	Data gap, no study on file
Reproduction, rat:	Data gap, no study on file
Teratology, rat:	Data gap, no study on file
Teratology, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect.

DNA damage: No data gap, no adverse effect
Neurotoxicity: Not required at this time

Toxicology one-liners are attached.

All records thorough # 073646 were examined.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

File name: T890808

Revised by Stanton Morris, 08/08/89.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

CHRONIC TOXICITY, RAT	No study on file.
CHRONIC TOXICITY, DOG	No study on file.
ONCOGENICITY, RAT	No study on file.
ONCOGENICITY, MOUSE	No study on file.
REPRODUCTION, RAT	No study on file.
TERATOLOGY, RAT	No study on file.
TERATOLOGY, RABBIT	50232-003; 046774 "Dose-range-finding-developmental Toxicity Study in Rabbits, 5601-56-1 (Naphthalene)" (Pharmakon Research International 10-85 Report no: PH 329DR-TX-001-85).

Naphthalene (>99.9% from synthesis information in CDFA Document 002), range-finding study for 46775 in New Zealand white rabbits at 0, 50, 250, 630 or 1000 mg/kg by oral gavage; 4 rabbits per group; 100% mortality at 630 and 1000 mg/kg; no developmental effects reported; 400 selected as the m.t.d. (Gee, 10/28/86; update, Shimer, 05/12/87).

** 50232-003; 046775; Developmental Toxicity Study in Rabbits, PH 329-TX-001-85, 5601-56-1, Order No.: J-277"; Pharmakon Research International, Inc., Waverly, NJ; Naphthalene, > 99.9%; Eighteen pregnant does / group were dosed by oral gavage with 0, 40, 200, or 400 mg/kg on gestation days 6-18. Signs of maternal toxicity included behavioral changes, diarrhea, and ocular and nasal discharge at 40, 200, and 400 mg/kg and reduced food intake at 400 mg/kg (NOEL < 40 mg/kg. No fetal effects were seen

(NOEL > 400 mg/kg). No adverse effect was demonstrated (fetal NOEL > maternal NOEL). The study was upgraded from unacceptable (Gee, 10/28/86; Morris, 11/22/88) to acceptable (Morris, 08/08/89).

50232-005; 063902: This record contained supplemental data on individual does and data related to analysis of dosing solution used in the study found at document # 50232-003, record # 046775. Examination of these data did not result in a change in study status and no worksheet was done (Morris, 11/22/88).

50232-008; 073646: This record contained supplemental data related to analysis of dosing solution used in the study found at document # 50232-003, record # 046775. Examination of these data resulted in upgrading of the study from unacceptable to acceptable (Morris, 08/08/89).

GENE MUTATION

50232-003; 046778 "Ames Salmonella/Microsome Plate Test (EPA/OECD), 5601-56-1 (Naphthalene)" (Pharmakon Research International Report No. PH 301-TX-020-85 11-26-85) Naphthalene [99.9% from CDFA Document 002]; Salmonella strains TA1535, TA1537, TA1538, TA98 and TA100 with and without rat liver activation, triplicate plates, single trial at 0, 3, 10, 30, 100 or 300.ug/plate in the plate incorporation assay; concentrations higher than 300 were judged toxic to TA1538 and TA100 in a preliminary toxicity screening. No increase in reversion rate is reported. UNACCEPTABLE (no repeat trial). (Gee, 10/28/86; update, Shimer, 05/12/87)

** 50232-006; 064790; "Ames Salmonella/Microsome Plate Test (EPA/OECD)," PH 301-TX-020-85, 5601-56-1, Order # J-270; Pharmakon Research International, Inc., Waverly, PA; 11/15/87; naphthalene, 99.8%; 3 replicates of 0.0, 3.0, 10.0, 30.0, 100, or 300 ug in 100 ul DMSO (final DMSO . 5%) / plate of Salmonella typhimurium TA1535, TA1537, TA1538, TA98, or TA100 tester strain, incubated for 48 hours at 37 :C, with or without S9 activation system from Aroclor-induced, male Sprague-Dawley rat livers; decrease in revertants at 300 ug/plate; adequate positive controls; no increase in revertants reported; no adverse effect; acceptable study; (Morris, 10/31/88).

CHROMOSOME EFFECTS

** 50232-003; 046777 "Micronucleus Test (MNT) OECD,5601-56-1 (Naphthalene)-Mouse" (Pharmakon Research International Report No: PH 309A-TX-007-85 10-31-85) Naphthalene [99.9% from CDFA Document 002], given once i.p. at 250 mg/kg to 5/sex/group CD-1 mice with sacrifice at 30, 48 and 72 hours; TEM as positive control; 250 was judged the m.t.d. from a preliminary test at 250, 500, 1666, 3000 and 5000 mg/kg -- all animals died at the 4 highest doses; no increase in micronuclei in polychromatic erythrocytes; trend toward a decrease in PCE/NCE with time.

ACCEPTABLE. (Gee, 10/28/86; update, Shimer, 05/12/87)

DNA DAMAGE

** 50232-003; 046779 "Rat Hepatocyte Primary Culture/DNA Repair Test, 5601-56-1 (Naphthalene)" (Pharmakon Research International Report no: PH 311-TX-008085 10-2-85) Unscheduled DNA synthesis in primary rat hepatocytes with naphthalene [99.9% from CDFA Document 002] tested at 0, 0.16, 0.5, 1.6, 5.0 or 16 ug/ml in triplicate wells; 60 cells (20 from each) were scored; concentrations selected from preliminary trial up to 5000 ug/ml; no induction of UDS is reported. ACCEPTABLE. (Gee, 10/28/86; update, Shimer, 05/12/87).