

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

TRIFORINE

Chemical Code # 1905, Tolerance # 00382
SB 950 # 243

Original date: August 5, 1986
Revised date 5/25/88, 7/11/88, 8/24/90, 5/05/93, 7/11/94

I. DATA GAP STATUS

Chronic, rat:	No data gap, no adverse effect
Chronic toxicity, dog:	No data gap, no adverse effect
Oncogenicity, mouse:	No data gap, possible adverse effect
Oncogenicity, rat:	No data gap, no adverse effect
Reproduction, rat:	No data gap, no adverse effect
Teratology, rat:	No data gap, no adverse effect
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.

In the one-liners below:

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

File name: T940711

Initial Summary prepared 8/5/86 by J. Gee. Revised 5/25/88 and 7/11/88 by Gee; Aldous,
8/24/90; Aldous, 5/05/93; Iyer, 7/11/94

All relevant reports indexed as of 4/23/93 were included in this Summary of Toxicology Data.
This includes all record numbers through 127022 and all document numbers through 382-111.
(Iyer, 7/11/94)

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

Considering the high dose range tested in Record No. 114579, the "possible adverse effect" identified in the 1974 study appears no longer relevant, being superceded by the more recent, more rigorous study. Aldous, 4/22/93.

382-098 114579 Perry, C.J., Mulhern, M., and Finch, J., "Triforine 104 week dietary carcinogenicity study in rats incorporating 52 week toxicity study". Inveresk Research International, Scotland, 7/23/91. Cr1:CD (SD) BR rats, 50/sex/group, were dosed in diet with 0, 200, 2000, or 20000 ppm triforine, 99.1% purity, for 104 wk. Mean achieved dosages were 10, 101, and 1038 mg/kg/day for males and 13, 136, and 1436 mg/kg/day for females. Groups of 20/sex/group were maintained for 52 wk as part of the chronic study component. NOEL = 200 ppm (slight b.w. decrement in males, slight increases in incidence or degree of "increased hemosiderin" or of "brown pigment deposits" in spleens of males and females at 2000 ppm). At 20000 ppm, modest changes in both sexes included b.w. decrements, hematology changes (reduced Hb and reduced RBC counts), increased liver weights, and increased Kupffer cell pigmentation. A small increase in spleen weights in females may have been treatment-related. The study is **acceptable, and no adverse effects are indicated. Aldous, 4/13/93.

382-074 072736 Protocol 382-098 114579, above.

008 976110 "Chronic Toxicity Test with the Compound (W-524-XX) in Rats using Oral Administration." (CH Boehringer Sohn & Johannes Gutenberg University, 6/74). Triforine (Lot T3/70, 96.6%) at 0, 25, 125, 625 or 3125 ppm in the diets of rats for 2 years; 50/sex for controls and high dose; 35/sex for other test groups. Systemic NOEL = 625 ppm (anemia: a **"possible adverse effect"**)--mild and inconsistent effect on red blood count, hematocrit and hemoglobin. No historical ranges were included. Incomplete (no diet analysis, no individual time to death data, etc.). UNACCEPTABLE. Registrant's response (letter of 4/9/87) states

that no stability data from this test are available; no raw data exist on diet analysis; no information was found on the frequency of diet preparation, no bone marrow smears or spinal cord sections. Initially considered upgradeable but now is not upgradeable for the above reasons. Harnois, 12/8/87 and Gee, 7/2/85 and 5/25/88 (no additional worksheet)

EPA one-liner: Systemic NOEL = 625 ppm. Core grade: minimum.

034 2092 & 2094 Very brief summary of 008 976110.

001 891059 (=38500) Very brief summary of 976110.

053 43951 & 43952 (CH Boehringer Sohn, 6/74) Supplemental information to 008 976110 --
Dose range-finding studies. Gee, 7/7/86.

054 43953 Full study report rewrite of 008 976110, with amended tables (missing some required data).

059 43960 (CH Boehringer Sohn, 6/74) Supplemental information to 008 976110.
Comments by Dr. Wilhelm of Celamerck. Gee, 7/7/86.

059 43962 (CH Boehringer Sohn, no date) Supplemental information to 008 976110.
Comments by Dr. Wilhelm of Celamerck. Gee, 7/7/86.

058 43958 & 43959 (C.H. Boehringer Sohn, 8/71) Triforine stability in water and purity data specified as for Batch 1. Supplemental information to 007 976108, 009 976115, 008 976110. Gee, 7/8/86.

CHRONIC TOXICITY, RAT
(see combined, rat, above)

CHRONIC TOXICITY, DOG

**382-007 976108 "Chronic Toxicity Test of the Substance, (W 524-XX) on Beagles, Oral Application over 104 Weeks." (CH Boehringer Sohn, 7/74). Triforine (W524-XX Lot T3/70, no purity) at 0, 10, 40, 100 or 1000 ppm in the diet for 104 weeks; 4/sex/group. NOEL = 100 ppm (siderosis of bone marrow and of liver Kupffer cells at 1000 ppm; enhanced erythropoiesis in bone marrows of 1000 ppm females). Study was considered unacceptable but upgradeable, due to inadequate characterization of test article, insufficient verification of administered dose, and lacking individual data (particularly on histopathology). Eventual upgrade to ACCEPTABLE followed submission of re-formatted report with individual data, plus retrospective diet analysis. Original review indicated a "possible adverse effect", citing bone marrow erythropoiesis (Remsen, 7/2/85). Findings at 1000 ppm were subsequently re-examined, and study was re-classified as not indicative of adverse effects (8/6/90 review). Gee, 8/7/86, 5/4/88 (no additional worksheet), Aldous, 8/6/90.

EPA one-liner: Systemic NOEL = 100 ppm. Core grade: minimum.

382-083 086429 (Addendum to study 007:976108) "W524-XX (Triforine): 104 Week Oral Toxicity Study in Dogs". Inveresk Research International, Scotland, August 1973. Data are reformatted to modern standards, and available individual data were presented. Additional retrospective analyses were provided to demonstrate that content, homogeneity, and stability were sufficient under conditions similar to the original study. The degree of toxicity at the high dose was determined in this re-examination not to be sufficiently high to warrant flagging a "possible adverse effect". The study should be re-classified as ACCEPTABLE, and no adverse effect is indicated. Kishiyama/C. Aldous, 8/6/90.

055 43954 & 43955 (C. H. Boehringer Sohn, 2/5/71). Subacute toxicity, dogs; results used for dosage selection for 007 976108. Subacute and 13-week oral studies in the dog.

056 43956 (C.H. Boehringer Sohn, 7/74) Full report for 007 976108; includes some individual data, frequency of diet preparation, stability in diet, results of diet analyses (3x) on top dose. Gee, 7/7/86.

059 43961 (C.H. Boehringer Sohn, 3/29/74) 7/3/86 Comments by Dr. Wilhelm of Celamerck. Supplemental to 007 976108. Gee, 7/3/86.

ONCOGENICITY, RAT
(see combined, rat, above)

ONCOGENICITY, MOUSE

****382-097 114319**, "Triforine: 105 week dietary carcinogenicity study in mice", Inveresk Research International, Scotland, August 14, 1991. (J. Heath, M. Mulhern, C.J. Perry, W. Henderson, IRI Project No. 437483, 8/14/91). Triforine, Batch Ch. 2764, 99.1%, was admixed into diets at concentrations of 0, 70, 700 or 7000 ppm and fed to 50 CrL:CD-1 (ICR) BR mice/sex/group for 105 weeks. NOEL = 70 ppm for males (diminished b.w. and diminished survival; pathology in colon and rectum (often fatal), consisting of thickened, enlarged, ulcerated or inflamed tissues). NOEL for females = 700 ppm (elevated liver weights, areas of hypertrophy in pancreas, brown pigment deposits in spleen). Oncogenicity findings included elevated alveolar/bronchiolar adenomas and carcinomas in 7000 ppm females, and small increases in hepatocellular tumors (notably carcinomas) in 700 ppm and 7000 ppm males. Degenerative changes in the lower intestines of 700 ppm and 7000 ppm males, alveolar/bronchiolar tumors in 7000 ppm females, and (to a lesser extent) hepatocellular tumors (particularly carcinomas) in 700-7000 ppm males are considered **"possible adverse effects"**. **Acceptable**. Kishiyama and Aldous, 4/22/93.

382-096 113911 Adverse effects report for 097:114319, above. Preliminary findings of liver tumors (males), lung tumors (females), and non-neoplastic pathology in colon and rectum of males were reported on 1/22/92 from Shell Internationale to the submitter, Biologic Inc. (No DPR review, since the final report is available). Aldous, 4/20/93.

382-100 119241 Veenstra, G. "Triforine: Discussion of weight-of-evidence for proposed carcinogenicity classification", 8/26/92. [Discussion relates to Record No. 114319, above]. Discussion covers several study types, but only the discussion on mouse oncogenicity is important, since the study had presented a "possible adverse effect". The submitted Discussion raised the question as to whether the higher two dose groups of males had been treated above the "MTD". There is no apparent reason to presume that increased deaths due to pathology of the lower intestine in mid-dose and high dose males had biased tumor data

incidence, however higher mortality in those groups requires that survival-adjusted analysis be performed. The Discussion presented reasons, most relevant to subsequent "weight of evidence" evaluation, why the increases in mouse liver and lung tumors may not be relevant to man. There is no change in study disposition as a result of this submission. Aldous, 4/26/93.

382-074 072735 [Protocol for "Carcinogenicity" study], D.J. Everett, Study Director. "78 Week dietary carcinogenicity study in mice". See CDFA comments by J. Gee in P890331. [Note: this presumably refers to study 097:114319, above. Due to high survival, the dosing period was extended. Aldous 4/23/93].

009 976115 "81-Week Carcinogenicity Study in Mice (Substance Administered in the Food) (W 524 - Triforine)." (CH Boehringer Sohn, 9/4/75) Triforine (lot T3/70, 96.6% ?) at 0, 30, 150 or 750 ppm in diets of 40 mice/sex/group for 81 weeks; NMRI-EMD-SPF mice. NOEL greater than 750 ppm. No adverse effect (oncogenicity or chronic) reported. Unacceptable (histopathology on 10 tissues only, dose selection not justified and no subchronic study to support selection). Prior review 7/2/85 by Gee. Not upgradeable (letter of 4/9/87 indicates diet analysis and data on stability in diet mix are not available, only the tissues listed in report were preserved.) Harnois, 12/8/87 and Gee, 5/25/88 (no additional worksheet).

EPA one-liner: Oncogenic NOEL: greater than 750 ppm. Core grade: guideline.

057 43957 (CH Boehringer, 9/4/75) Supplemental information to 009 976115: List of all mice autopsied, histopathology records, historical control data, amendments. Gee, 7/8/86.

059 43963 (CH Boehringer, 9/4/75) Supplemental information to 009 976115. Comments by Dr. Wilhelm of Celamerck. Gee, 7/8/86.

REPRODUCTION, RAT

382-109 127020, "Triforine: Two Generation Reproduction Study in Rats", Supplementary Histology Report. (K.P. Hazelden and R. Aitken, Inveresk Research International, IRI Project

No. 437656, 09/23/92). Triforine, purity 99.1%, admixed with the diet at 0, 500, 3000 or 20000 ppm, fed to two generations of Sprague-Dawley rats (28 rats/sex/group for F0 generation; 24 rats/sex/group for the F1 rats; 1 litter per generation). Body weight gains and food consumption decreased slightly in 20000 ppm adults. In both generations and both sexes a consistent, dose-related increases in liver weights were noted at 3000 and 20000 ppm. Histopathology revealed extra medullary hemopoiesis and hemosiderosis in the spleen along with an increase in splenic weight at both 3000 and 20000 ppm (F0 and F1); nephropathy, nephrocalcinosis (females) along with an increase in kidney weights at all dose levels of triforine administered (F0 and F1) and very active appearance of thyroid cells in females (20000 ppm) with increased thyroid weights at both 3000 and 20000 ppm. Apparent parental NOEL = 500 ppm. Apparent reproduction or pup NOEL = 3000 ppm, based on above findings. **No apparent adverse effects.** **Acceptable** (P. Iyer, 1/14/93).

** 382-095 111063, "Triforine: Two Generation Reproduction Study in Rats", (C. McCay and K.P. Hazelden, Inveresk Research International, IRI Project No. 437656, 10/12/90). Triforine, purity 99.1%, admixed with the diet at 0, 500, 3000 or 20000 ppm, fed to 28 Sprague-Dawley rats/sex/group in the F0 generation (24/sex/group for the F1 rats). Body weight gains and food consumption decreased slightly in 20000 ppm adults. Consistent, dose-related increases in liver weights were noted in adults at 3000 and 20000 ppm. The only notable effect on offspring was a 20% weight gain decrement in 20000 ppm pups during lactation. Apparent parental NOEL = 500 ppm. Apparent reproduction/pup NOEL = 3000, based on above findings. **No apparent adverse effects.** Initially received as **Unacceptable** (no histology on F1 adults). A detailed worksheet will be done when the required histology data are submitted. Kishiyama and Aldous, 5/05/93. See #127020 in 109 for the histopathology report which upgrades the study to **acceptable** status.

382-074 072737 [Protocol for reproduction study]. K. P. Hazelden, Study Director. "Two generation reproduction study in rats". See CDFA comments by J. Gee in P890331.

009 976118 "Three Generation Study with the Fungicide W 524 (Triforine) in Rats." (CH Boehringer Sohn, 5/31/74) Triforine (99.4%) at 0, 100, 500 or 2500 ppm in the diet; 10 males and 20 females per dose, 3 generations, 2 litters per generation; Insufficient high

dose, histopathological exam too limited - no tissues from parental breeders; NOEL greater than 2500 ppm; Incomplete, UNACCEPTABLE. Letter of 4/9/87 indicated that a new study would be performed. Gee, 7/3/85 and 5/25/88.

EPA one-liner: Reproductive NOEL = 2500 ppm. Core grade = not stated.

059 43964 (C.H. Boehringer Sohn, 5/3/74) Supplemental information to 009 976118; Comments by Dr. Wilhelm of Celamerck. Gee, 7/8/86.

TERATOLOGY, RAT

** 110 127021 Fuchs, A., "Oral (Gavage) Teratogenicity Study in the Rat" (Hazleton, Project No. 121-006, 11/6/93). Triforine, batch 2764, 97.8%, administered to bred Sprague-Dawley Crl: (SD)BR rats, orally (gavage) at 0 (distilled water), 200, 500 or 1000 mg/kg/day on days 6 - 15 of gestation, 30/group. NOEL (maternal) > 1000 mg/kg. All developmental parameters were comparable to control. No teratogenic effects were observed. Rationale for dose selection not included, but 1000 mg/kg is considered a "limit" test. **Acceptable.** (P. Iyer, 12/28/93).

** 009 976116 "Effects of W-524 (Triforine), Lot 1, on Pregnant Rats and Their Fetuses, Following Oral Administration." (Laboratorium Für Pharmakologie und Toxikologie, 4/14/72). Additional information (see 059 43965). Triforine (99.4%) at 0, 100, 400, 800 or 1600 mg/kg by oral gavage. Increase in number of resorptions, increase in number of fetal variations (ossification of sternbrae); developmental NOEL = 400 mg/kg (decreased litter size and increased resorptions). Maternal NOEL greater than 1600 mg/kg. Complete and ACCEPTABLE. Possible adverse effect. Gee, 7/3/85 and 7/9/86.

EPA one-liner: Teratogenic NOEL greater than or equal to 1600 mg/kg (HDT) Fetotoxic NOEL = 800 mg/kg, Core grade = minimum.

059 43965 (Laboratorium Für Pharmakologie und Toxikologie, 4/14/72). Supplemental information to 009 976116. Upgrades 976116 to ACCEPTABLE status. Includes comments by Dr. Wilhelm of Celamerck. Gee, 7/9/86.

The findings of retarded ossification of the sternabrae at 800 mg/kg and higher doses in the earlier study (# 0976116) were not repeated in the recent study (# 127021) at 1000 mg/kg. Additionally, while decreased litter size and increased resorptions were noted at the 1600 mg/kg dose in the previous study (# 0976116) a similar trend was not observed at the 1000 mg/kg dose level in the recent study (# 127021). The possible adverse effects were thus not confirmed at comparable doses. Hence Maternal NOEL > 1000 mg/kg and Developmental NOEL = 1000 mg/kg (based on #127021) (Iyer, 7/11/94).

TERATOLOGY, RABBIT

111 127022, "Triforine: Oral (Gavage) Teratogenicity Study in the Rabbit", (A. Fuchs, Hazleton Laboratories Deutschland GmbH, Laboratory ID. 121-004, 6/14/93). Triforine (97.8 % purity), Batch 2764, at concentrations of 0 (distilled water) or 1000 mg/kg was administered orally (gavage) to 18 mated female New Zealand rabbits/group/day during days 6 through 18 of gestation. A reduction in the mean maternal body weight gain during treatment along with reduced daily food consumption was noted. There was no evidence of implantation effects or teratogenicity. However, embryotoxicity as evidenced by reduced fetal weight, was observed in the group exposed to triforine. Additionally, incomplete ossification of the bones of the extremities and pelvic girdle was also noted in some fetuses in the treated group. Maternal NOEL < 1000 mg/kg; Developmental NOEL < 1000 mg/kg. Unacceptable (single dose of limit test without NOEL's). (P. Iyer, 1/18/94).

NOTE: Earlier studies (#'s 087609 and 37757) indicate a developmental NOEL \geq 150 mg/kg. The pilot study (# 098868) did not identify developmental effects at 100, 300 or 1000 mg/kg/day by gross examination. Collective data from these several studies are adequate to describe potential developmental toxicity.

NOTE: Studies prior to this time (4/23/93) are shown below to have had maternal NOELs well below the 1000 mg/kg/day high dose proposed for the upcoming study, yet these studies have been faulted for failure to adequately challenge the does. The apparent discrepancy lies in

the fact that maternal toxicity does not appear to be marked at any dose, up to the "limit test" dosage level of 1000 mg/kg/day. Aldous, 4/23/93.

382-093 098868, "Triforine: Preliminary Oral (Gavage) Embryotoxicity Study in the Rabbit", (W. Müller, Hazleton Laboratories Deutschland GMBH, Laboratory ID# 121-003, 8/27/91). Triforine, 0, 250, 500, or 1000 mg/kg was administered by gavage to 8 mated female New Zealand rabbits/group during days 6 through 18 of gestation. Modest body weight reduction was found in does, particularly at dosing initiation, for all triforine groups. Food consumption appeared reduced for mid and high dose groups. No strong indications of maternal or developmental toxicity (fetuses were examined only grossly). The investigators considered 1000, 300, and 100 mg/kg/day suitable for a main teratology study, which appears justifiable. No DPR review is needed for this pilot study. (Kishiyama and Aldous, 4/23/93).

077 087609 Müller, W., "Oral (Gavage) Teratogenicity Study in the Rabbit" (Hazleton, Project No. 460/29, 4/27/89). Triforine, batch 2764, 98.1%, was administered to bred New Zealand White rabbits at 0 (distilled water), 6.0, 30.0 or 150.0 mg/kg on days 6 - 18 of gestation, 18/group. NOAEL (maternal) > 150 mg/kg. Apparent NOEL (maternal) = 30 mg/kg (primarily based on decreased maternal food consumption of 150 mg/kg/day dams, which was statistically significant during p.c. days 12-18). NOEL (developmental) > 150 mg/kg. All reproductive parameters were comparable to control. No adverse effects. UNACCEPTABLE. A defensible high dose was not achieved. Shimer/C. Aldous, 8/23/90.

382-077 087610 Analysis of triforine Batch 2764, used in study 87609.

048 37757 "Teratogenicity Study in Himalayan Rabbits after Oral Administration." (E. Merck, Darmstadt, Germany, 2/20/81) Triforine technical (no purity) at 0, 5, 25 or 125 mg/kg by oral gavage; days 6 to 18; 15 does bred per group but only 9, 8, 12 and 10 were pregnant for control through high dose groups respectively; Maternal toxicity NOEL = 5 mg/kg; developmental toxicity NOEL ≥ 125 mg/kg; No teratogenic effect reported. UNACCEPTABLE (too few litters, pups, no analysis of dosing solutions, doses not justified). Gee, 2/3/86. (Harnois, 12/8/87).

EPA one-liner: Teratogenic NOEL greater than or equal to 125 mg/kg;

Maternal NOEL = 5 mg/kg;

Fetotoxic NOEL = 5 mg/kg;

Core grade = Minimum.

382-076 087608 Exact duplicate of 382-048:037757.

GENE MUTATION

** 047 37754 "In vitro Assessment for Mutagenic Potential in Bacteria with and without Addition of a Metabolizing System (Salmonella typhimurium)." (E. Merck, Darmstadt, Germany, 3/25/85) Salmonella typhimurium; Triforine (99.9%) at 0, 10, 50, 250, 1250, 2500 and 5000 ug/plate \pm S9; 4 replicates, two trials with each strain; no increase in reversion rate. ACCEPTABLE. Gee, 1/31/86.

No EPA one-liner available.

** 047 37758 "Mutations Affecting the Hypoxanthine-Guanine Phosphoribosyl Transferase Locus in V79 Cells." (Technical University, Darmstadt, Germany, 12/12/84) Chinese hamster V79 HGPRT; Triforine (99.9%) at 0, 5, 10, 25, 50 ug/ml, 4 hours with and without rat liver activation; two trials; no increase in mutation frequency. Complete, ACCEPTABLE. Gee, 1/31/86.

No EPA one-liner available.

021 976120 "Evaluation of Three Compounds for Their Mutagenic Potential Utilizing Ames Methodology (Technical Triforine) with and without Added Metabolizing System." (Huntingdon Research Center, 6/6/78) Salmonella typhimurium (TA 1537, TA 1535, TA 1538, TA 98, TA 100); MPY-C, 100% (N-methyl-2-pyrrolidone, an "inert" compound in "Funginex" at 0, 1, 10, 100 or 1000 ug/plate; single plates, plus and minus S9; Incomplete; UNACCEPTABLE: major variances. Gee, 7/3/85.

No EPA one-liner available.

011 32740 "Triforine Trial for Mutagenic Potential in Bacteria with and without added Metabolizing System." (Germany Institute of Toxicology, 9/8/77) Salmonella typhimurium (TA 98, TA 100); Triforine, technical (Lot 1/75); 0, 0.002, 0.02, 0.2, 2.0, 10.0, 20, 100 or 200 micromoles/plate; plus and minus S9 (phenobarbital induced); inadequate positive control response with TA 100, only two strains used; Incomplete; UNACCEPTABLE: major variances. Gee, 7/3/85.

No EPA one-liner available.

CHROMOSOME EFFECTS

** 047 37755 "Chromosome Aberrations in Cells of Chinese Hamster Cell Line V79." (Technical University, Darmstadt, Germany, 8/15/85) Chromosome aberrations in Chinese hamster V79; Merck, 1985; Triforine (99.9%) at 0, 5, 40, and 50 ug/ml, -S9; at 0, 4, 25 & 40 ug/ml +S9, 4 hours, harvest at 7, 18 or 28 hours: No increase in aberrations reported. Complete, ACCEPTABLE. Gee, 1/31/86.

No EPA one-liner available.

036 25226 "Mouse Micronucleus Assay With Triforine." (Research & Consulting Company AG, Switz., 1/11/84). In vivo bone marrow: mouse; Triforine (98.8%) was administered once by oral gavage at 0 or 5000 mg/kg (50 mg/kg cyclophosphamide, positive control); bone marrow sampled at 24, 48 & 72 hours from 5 animals/sex/group; high dose inadequate; at 48 hours, females appeared to have a statistically significant increase in micronuclei; PCE/NCE was also higher at 24 and 48 hours in females; in the repeat study, no such effect was found (see record #25227); UNACCEPTABLE: major variances. Gee, 7/3/85.

No EPA one-liner available.

036 25227 "Mouse Micronucleus Assay with Triforine." (Research & Consulting Company AG, Switz., 6/6/84). In vivo bone marrow: mouse. Triforine technical (98.8%) was administered once by oral gavage at 0, 200, 1000 or 5000 mg/kg (50 mg/kg cyclophosphamide, positive control); repeat of 48 hour sample (see record #25226) in female mice; Incomplete; UNACCEPTABLE: major variances (high dose inadequate). Gee, 7/3/85.

No EPA one-liner available.

NOTE: No adverse effects were observed for chromosomal effects in vitro; the positive findings observed only in females and only at 48 hrs were not reproducible. The available data do not indicate that adverse effects resulted from the test substance.

DNA DAMAGE

** 047 37756 "Unscheduled DNA Synthesis in Hepatocytes of Male Rats in vitro." (Technical University, Darmstadt, Germany, 2/13/85) Unscheduled DNA synthesis in rat hepatocytes; Triforine Technical (99.9%) at 0, 0.5, 1.0, 10.0 25.0 and 50.0 ug/ml, 6 cultures per concentration; DPM/ug DNA: no increase with test article. ADEQUATE; Complete. Gee, 2/3/86.
No EPA one-liner available.

NEUROTOXICITY

Not required at this time.