CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

CYPHENOTHRIN

Chemical Code # 3885, Tolerance # 51975
SB 950 # New A.I.

Original date: 6/8/94
Revised date: 5/1/95

I. DATA GAP STATUS

Chronic toxicity, rat: No data gap; no adverse effects
Chronic toxicity, dog: No data gap; possible adverse effects
Oncogenicity, rat: No data gap; no adverse effects
Oncogenicity, mouse: No data gap; no adverse effects
Reproduction, rat: No data gap; no adverse effects
Teratology, rat: No data gap; no adverse effects
Teratology, rabbit: No data gap; no adverse effects
<table>
<thead>
<tr>
<th>Toxicology One-Liners</th>
<th>Attached</th>
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All record numbers through 134725 were examined.
** indicates an acceptable study.
**Bold face** indicates a possible adverse effect.
## indicates a study on file but not yet reviewed.

File name: t951050

Revised by: Charles D. Miller; 5/1/95
II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

COMBINED, RAT

** 51975-015; 119979, 123684, 123686, 123688; "S-2703F Combined Chronic Toxicity/Oncogenicity Study in Rats"; P.A. Martin; Life Science Research, Eye, Suffolk, England; Project No. EET-81-0084; 9/28/88 (Study Amendments); S-2703 Forte (Lot No. PY-83024, 95.2% Cyphenothrin); 0, 100, 300, 1,000 ppm (averaged intake (M) 0, 5, 15, 48, and (F) 0, 6, 18, 59 mg/kg/day, respectively) in diets; dose concentrations selection based on results of 13 week study (see Rec. # 119964); 80 rats/sex/dose; observations- no treatment related increase in mortalities, demonstration of clinical signs or consistent dose-dependent changes in water consumption, ophthalmology, urinalysis, hematology or clinical chemistry occurred; in the oncogenicity portion of the study slightly decreased body weight gain and food consumption was noted in the 1000 ppm level females, NOEL (M/F) >1000 ppm (based on no treatment related effects); No Adverse Effect; Study acceptable. (Miller, 4/18/94)

CHRONIC TOXICITY, RAT

See Combined, Rat

CHRONIC TOXICITY, DOG
"Chronic (52 week) Oral Toxicity Study of S-2703F in Beagles" [Author: R. Nagata; Shin Nippon Biochemical Laboratories, Ltd.; Project No. EET-81-0085; 11/25/88; S-2703 Forte (94.2% Cyphenothrin)]; 0, 3, 10, 30, 60 mg/kg in gelatin capsules; 4 dogs/sex/dose; observations— one high dose female death; high dose animals clinical signs included tremors, convulsions, pale or reddened oral mucosa and conjunctiva, decreased spontaneous movement, salivation, emesis, and diarrhea, in the 30 mg/kg animals tremors, pale oral mucosas, and decreased spontaneous movements were noted, the 10 mg/kg animals exhibited vomiting and reddened oral mucosas and conjunctivas; a slight decrease in food consumption was noted in the high dose animals; no other treatment related effects were noted in any other parameter; no abnormal macroscopic or microscopic observations; NOEL (M/F) = 3 mg/kg (based on clinical signs); **Possible adverse health effects**: Tremors and convulsions at 30 mg/kg and higher; **Study acceptable.** (Miller, 3/15/94)

ONCOGENICITY, RAT

See Combined, Rat
ONCOGENICITY, MOUSE

** 51975-016; 119980, 123689; "S-2703F: Oncogenicity Study by Dietary administration to B6C3F1 Mice for 104 Weeks"; P.A. Martin; Life Science Research, Eye, Suffolk, England; Project No. EET-91-0091; 8/17/89; S-2703F (Lot No. PKG 84036, 94.6-94.9% cyphenothrin); 0, 100, 300, 1,000 ppm in diets; 80 mice/sex/dose; dose concentrations were justified with results from a 13 week (see Rec. # 119963) preliminary dietary study that showed some deaths at doses of 1000 and 2000 ppm; in the main study 19% of the males and 24% of the females survived until the end of week 104; survival was unaffected by treatment; observations- no treatment-related clinical signs were noted; absolute and bodyweight-relative kidney weights were lower but not significantly different among male animals which received 300 or 1000 ppm when compared to controls; no treatment related changes were observed in clinical chemistries, at necropsy or histopathological examinations; no statistically significant increased incidence of neoplasms associated with treatment were observed; no adverse effects; NOEL (M/F)= 1000 ppm (based on no treatment-related effects); Study acceptable. (Miller, 4/15/94)

REPRODUCTION, RAT

** 51975-018, 019; 119986, 119988; "S-2703F: Effects Upon Reproductive Performance of Rats Treated Continuously Throughout Two Successive Generations" (Author: J. M. Tesh; Life Science Research, Eye, Suffolk, England, Project No. EET-61-0067, 10/21/86); S-2703 Forte (93.6% Cyphenothrin); 0, 100, 300, 1000 ppm dietary; 24 CD rats/sex/dose both F1 and F2 observations-no dose related mortalities were observed, statistically significant lower body weight gains were observed in F1 high dose females, no additional statistically significant differences were found in other adult parameters; there were no significant differences in any clinical observations in the F1 and F2 pups; generally gross necropsy and histomorphologic findings of
adults and offspring were few and were not considered treatment related; Adult NOEL = 300 ppm of a.i. (based on decreased body weight gain) Developmental NOEL = 1000 ppm of a.i. (based on no treatment related effects); Acceptable. (Miller, 3/2/94)

TERATOLOGY, RAT

** 51975-017, -024; 119985, 134720, -721, -722; "Teratogenicity Study in Rats Treated Subcutaneously with S-2703 Forte" (Author: K. Yamanouchi et al; Bozo Research Center Inc., Shizuoka, Japan, Project No. EET-41-0026, 1/24/95); S-2703 Forte (Lot # PK 81051, 93.6% Cyphenothrin); 0, 50, 150, 500 mg/kg/day administered subcutaneously on days 7 to 17 of gestation; 38 female rats/dose; observations- Maternal effects: a significant decrease in weight gain was shown in the high dose group; no teratogenic effects attributable to the test substance were noted, Fetal effects: no physiological or developmental effects were observed at any dose level; Maternal NOEL = 150 mg/kg (based on decreased weight gain), Developmental NOEL = 500 mg/kg (based on no effects); no adverse effects; Study initially reviewed as unacceptable but possibly upgradeable (Miller, 4/6/94); study re-reviewed with dose solutions analytical data and gas chromatographic validation data; acceptable (upgraded, Miller, 4/23/95).
TERATOLOGY, RABBIT

51975-017; 119982, 123694; "Teratogenic Study of S-2703 Forte in Rabbits"; Y. Nagashima et al.; Bozo Research Center Inc., Shizuoka, Japan. Project No. EET-41-0029, 5/31/84); S-2703 Forte (Lot PK-81051, 93.6% Cyphenothrin); 0, 25, 50, 125 mg/kg/day administered subcutaneously on days 6 to 18 of gestation; 15 New Zealand White female rabbits/dose; observations- Maternal effects: a significant decrease in feed consumption was shown in the high dose group, no reproductive or teratogenic effects attributable to test substance were noted; Fetal effects: no physiological or developmental effects were observed at any dose level; Maternal NOEL = Developmental NOEL = 125 mg/kg (based on no effects at HDT); no adverse effects; unacceptable, not upgradeable. (Miller, 4/5/94)

** 51975-017, -024; 119983, 134719, -721, -722; "Teratogenic Study of S-2703 Forte in Rabbits" (Author: Y. Nagashima et al; Bozo Research Center Inc. Shizuoka, Japan, Project No. EET-41-0036, 1/24/95); S-2703 Forte (Lot # PY 83024, 95.7% Cyphenothrin); 0, 50, 125 mg/kg/day administered subcutaneously on days 6-18 of gestation and 250 mg/kg/day on days 6-10 of gestation; 15 New Zealand White female rabbits/dose; observations- Maternal effects: a significant decrease in body weight was shown in the two high dose groups, no reproductive or teratogenic effects attributable to test substance were noted; Fetal effects: no physiological or developmental effects were observed at any dose level; Maternal NOEL = 50 mg/kg (based on decreased body weight), Developmental NOEL = 250 mg/kg based on no effects); no adverse effects; study initially reviewed as unacceptable but possibly upgradeable (Miller, 4/6/94) study re-reviewed with dose solutions analytical data and gas chromatographic validation data; acceptable (upgraded, Miller, 4/27/95)

RABBIT TERATOLOGY SUMMARY
In the initial study a subcutaneous route of administration was utilized and the highest dose level (125 mg/kg/day) failed to induce any overt maternal toxicity. In a second upgraded rabbit study a higher dose level (250 mg/kg/day), administered subcutaneously, was utilized producing maternal toxicity (Miller, 4/27/95).

**GENE MUTATION**

** 51975-020, 119990; "Gene Mutation Test of S-2703 Forte in Bacterial System" (Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report No. EET-20-0008, 10/21/82); S-2703 Forte, (Lot No. PK-81051, 93.6% purity), tested with Salmonella typhimurium strains TA-1535, TA-1537, TA-1538, TA-98 and TA-100 and Escherichia coli WP-2 uvrA in the presence and absence of rat liver metabolizing enzyme system (S9 mix); duplicate plates, two trials for nonactivated and activated systems; 20 minute preincubation before plating; dose range 0-5000 ug/plate; 48 hour incubation; no increase in reversion rate reported; no adverse effects indicated; acceptable; (Miller, 4/18/94).
CHROMOSOME EFFECTS

** 51975-020, 119991; "Micronucleus Test of S-2703 Forte" (Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report No. EET-30-002, 10/11/83); S-2703 Forte, (Lot No. PK-81051, 93.6% purity), tested in mouse bone marrow erythrocytes; ICR mice; 6 mice/dose; doses 0, 200, 400, and 800 mg/kg; mitomycin C 2 mg/kg positive control; bone marrow samples taken 24, 48 and 72 hours after dosing with 800 mg/kg and at 24 hours following dosing with 200, 400, 800 mg/kg and positive control; test article did not produce an increase in induced micronuclei in mouse bone marrow erythrocytes; **no adverse effects indicated; acceptable**; (Miller, 4/18/94).

Other Genotoxic Effects

** 51975-020, 119992; "In vitro Sister Chromatid Exchanges Test of S-2703 Forte in CHO-K1 cells" (Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report No. EET-30-022, 11/15/83); S-2703 Forte, (Lot No. PK-81051, 93.6% purity), tested in Chinese hamster ovary cells with and without S9 mix; 50 cells per dose; dose range 10^{-7} to 10^{-3} moles; 2 hour treatment; test article did not cause an increase in sister chromatid exchanges in cultured Chinese hamster ovary cells; **no adverse effects indicated; acceptable**; (Miller, 4/18/94).

NEUROTOXICITY

Not required for this product at this time.