

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

FENPROPATHRIN

Chemical Code # 2234, Tolerance # 50489
SB 950 # 349

3/12/91

I. DATA GAP STATUS

Combined, rat:	No data gap, possible adverse effect (not oncogenic)
Chronic toxicity, dog:	No data gap, possible adverse effect
Oncogenicity, mouse:	No data gap, no adverse effect
Reproduction, rat:	No data gap, possible adverse effect (not reproductive)
Teratology, rat:	No data gap, possible adverse effect (not developmental)
Teratology, rabbit:	No data gap, possible adverse effect (not developmental)
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 for this compound - but an inadequate study, possible adverse effect indicated

Toxicology one-liners are attached.

All record numbers through 91154 were examined.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

indicates a study on file but not yet reviewed.

File name: T910129

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

COMBINED, RAT

**** 058; 91138;** "S-3206 Potential Tumorigenic and Toxic Effects in Prolonged Dietary Administration to Rats" (Huntingdon Research Centre, Ltd., England, Report No. FT-61-0161, 7/15/86); 835; CD rats; S-3206 technical grade (91.4-92.5% purity) in diet; 0, 50, 150, 450, or 600 ppm to 50 rats/sex/dose; satellite groups: 15 rats/sex/dose; 600 ppm female group was terminated after 52 weeks due to increased mortality rate among males and females receiving 600 ppm and females receiving 450 ppm during first 26 weeks; **possible adverse effect:** body tremors observed among females receiving 600 ppm and to a lesser extent in males receiving 600 ppm and females receiving 450 ppm between weeks 2 and 52; no tumorigenic effects arising from treatment with S-3206; no compound-related effects on food consumption, body weight changes, hematology, clinical chemistry, necropsy and histopathology; NOEL (F) = 150 ppm, (M) = 450 ppm based on body tremors and mortality rate; **acceptable;** (Leung, 12/7/90).

CHRONIC TOXICITY, RAT

006, 010; 9806, 9807, 9854; "Toxicity Studies on the Insecticide WL-41706: Results of physical appearance, survival, body weight, food intake, organ weights, clinical chemistry, hematology and gross pathological observations of rats exposed to WL-41706 for up to two years" (Shell Research Limited, London, UK, Lab. Report No. FT-91-0026, FT-11-0046, FT-10-0048, 12/17/79); 831; COBS rats; WL-41706 (97% purity); 0, 1, 5, 25, 125, 500 ppm in diet for 104 weeks; 24 rats/sex/dose for a.i.; 48 rats/sex for controls; **no adverse effects indicated;** no treatment-related effects were reported in body weights, food intake, survival, clinical chemistry, and hematology; no significant chronic toxic effects attributed to long term feeding of WL-41706 were detected on the basis of macroscopic observation and histopathological examination; increases in spleen (6 months), heart (6 months), and liver (2 years) weights in 125 and 500 ppm female groups; NOEL (M/F) \geq 500 ppm; insufficient dose level and appendices cited in text (record # 9807) were missing; study **unacceptable** and **not upgradeable;** (de Vlaming and Gee, 10/29/85; updated Leung, 12/3/90)

052 91132; "Stability of S-3206 in the Diet" (Sumitomo Chemical Co., Ltd., Laboratory of Biochemistry & Toxicology, Hyogo, Japan, Lab. Report No. FP-00-0008, 11/80); S-3206, suspended in corn oil, was mixed with standard feed (final concentration: 300 and 600 ppm) and stored in polyethylene bag at room temperature (20-28°) for two weeks; stability analysis showed that S-3206 in diet was stable (96.8 - 99.8% of original amount) for two weeks at room temperature; **Supplemental;** (Leung, 11/16/90).

CHRONIC TOXICITY, DOG

**** 010, 014, 059; 9851, 33916, 91139;** "Chronic Toxicity Study in Dogs S-3206 T.G." (Hazleton Laboratories America, Inc., Vienna, VA, Lab. Report No. FT-41-0122, 11/12/84); beagle dogs; 831; S-3206 (technical grade, Lot # 20514, 92.5% purity) in diet; 0, 100, 250, or 750 ppm to 4 dogs/sex/dose; slightly lower mean body weights for high-dose dogs throughout study; no treatment-related changes reported in food consumption, hematology, clinical chemistry, urinalysis, ophthalmology, gross pathology, and histopathology; clinical signs: one high-dose male found dead during week 32 of study had exhibited ataxia and tremors prior to death; **possible adverse effects:** tremors observed consistently for high-dose dogs and sporadically for mid-dose dogs throughout study; ataxia and languidity noted for high-dose dogs throughout study; NOEL (M/F) = 100 ppm based on tremors, ataxia and languidity; study was originally reviewed and found to be unacceptable but possibly upgradeable with submission of missing appendices (de Vlaming and Gee, 10/30/85); this study was rereviewed with the cited appendices and was found to be **acceptable** (upgraded, Leung, 12/5/90)

ONCOGENICITY, MOUSE

**** 060; 91140;** "S-3206 Two-Year Feeding Study in Mice" (Huntingdon Research Centre, Ltd., England, Lab. Report No. FT-51-0135, 12/3/85); 832; CD-1 mice; S-3206 technical grade (91.4-92.5% purity) in diet; 0, 40, 150, or 600 ppm to 52 mice/sex/dose; satellite groups: 40 mice/sex/dose; **no adverse effect;** no treatment-related effects on mortality, body weight gain, organ weights, food consumption, efficiency of food utilization, hematological indices, urinalysis, biochemistry and neoplastic lesions; NOEL (M/F) \geq 600 ppm (no effect at HDT) **acceptable;** (Leung, (12/12/90).

061; 91141; "S-3206 Two-Year Feeding Study in Mice: (Terminated after 13 Weeks of Treatment)" (Huntingdon Research Centre, Ltd., England, Lab. Report No. FT-21-0073, 11/82); 832; CD-1 mice; S-3206 (technical grade, 91.4% purity) in diet; 0, 40, 200, or 1000 ppm to 52 mice/sex/dose; satellite groups: 40 mice/sex/dose; study was terminated after 13 weeks of treatment due to high mortality reported among mice receiving 200 or 1000 ppm during the early part of study; **possible adverse effect indicated:** occasional body tremor noted for a few males receiving 1000 ppm from week 1 onwards and for 1 male receiving 200 ppm in week 2; increased (15 - 16 g, $p < 0.05$) body weight gain for males receiving 200 or 1000 ppm; slightly higher liver weights for males and females treated at 1000 ppm; no treatment-related effect on food utilization and morphological changes at histological exam were detected; NOEL (M) = 40 ppm (increased mortality and body tremor), (F) = 200 ppm (increased mortality); **supplemental;** (Leung, 12/10/90).

REPRODUCTION, RAT

010, 066, 067, 068; 9852, 9853, 91146, 91147, 91148; "Toxicity Studies on the Insecticide WL-41706: Three Generation Reproduction Study (minus histo- pathology) in Rats"; (Histopathology data in 068) (Shell Research Ltd., UK (Histopathology - Inveresk Research International, UK, FT-91-0027, 12/17/79); COBS rats; 834; WL-41706 (batch no. 26C, 97% purity); 0, 5, 25, or 250 ppm in diet to 30 rats/sex/group per parental generation - 3 generation study; **no adverse effects indicated**; no compound-related changes in parental body weight, food consumption, and reproductive indices; small reduction in litter size in 250 ppm F-1a litter ($p < 0.05$, 89.8% of control) but absent in subsequent top dose litters and therefore not toxicologically relevant; changes in pup weight were inconsistent with respect to time and magnitude; pathological examination revealed hydrocephalus in 250 ppm pups from F-1b litters (1/329, $p = 0.475$) and 5 ppm and 250 ppm pups from F-3b litters (1/135, $p = 0.369$ and 1/212, $p = 0.479$; respectively); maternal NOEL = developmental NOEL \geq 250 ppm; insufficient dose level selection; study **unacceptable** and **not upgradeable**; (de Vlaming and Gee, 11/4/85; updated Leung, 1/7/91).

**** 069; 91149, 91150**; "Effect of S-3206 on Multiple Generations of the Rat" (Huntingdon Research Centre, Huntingdon, England, Lab. Report No. FT-61-0159, 7/4/86); COBS rat; 834; S-3206 (batch no. 20514, 92.5% purity); 0, 40, 120, or 360 ppm in diet to 17-28 rats/sex/group per parental generation - 3 generation study; no effect on mating performance of surviving animals; no mortality among males; **possible adverse effect**: dose-related mortality in F-1b generation females during lactation at mid and high dose; second and third week post partum females exhibited body tremors with associated spasmodic muscle twitches and increased sensitivity at high and mid dose levels; three F2b pups at mid dose showed body tremors prior to weaning, two of which subsequently died; histopathological examination did not reveal any abnormalities associated with treatment; maternal NOEL = 40 ppm (based on tremors and unscheduled deaths), paternal NOEL \geq 360 (no effect at HDT); systemic NOEL = 40 ppm (based on F2b pups at mid dose showing tremors); reproductive NOEL = 120 ppm (based on decreased litter size and pup weight); study **acceptable**; (Leung, 1/9/91)

TERATOLOGY, RAT

008, 062; 9840, 91142; "Teratology Study in Rats, Final Report" (Hazleton Laboratories America, Inc., Vienna, VA, Lab. Report # FT-01-0031 with addendum, 9/87); Fischer 344 Rats; 833; S-3206 (lot# 90403, 96.2% purity); oral intubation; 0, 0.4, 2.0, 10 mg/kg/day in corn oil to 27-28 females/dose on days 6-15 of gestation; **possible adverse effects indicated**: tremors observed in some high dosed females following first dose and one subsequent day during the treatment

period; mortality in one mid-dose and nine high-dose females (including 2 of which were not pregnant); decrease in body weight gain (73% of control, $p < 0.05$) due to reduced food consumption (85% of control, $p < 0.05$) at HDT during treatment period; increased incidence of clinical signs (blood crust on eye, lacrimation, and red eye) reported for HDT; fetal death observed in the litter of one control and one mid-dose female; one dead fetus (control) appeared edematous and another dead fetus (mid dose) was edematous and exhibited hydrocephaly and gastroschisis; maternal NOEL = 0.4 mg/kg/day (based on tremors and unscheduled death); developmental NOEL ≥ 10.0 mg/kg/day (no effect at HDT); study was originally unacceptable but possibly upgradeable of missing appendices and individual data (de Vlaming and Gee, 11/4/85); study **unacceptable** but **possibly upgradeable** with submission of dose analysis; (Leung, 12/26/90).

**** 063; 91143;** "Rat Teratology Study with S-3206" (Hazleton Laboratories America, Inc., Vienna, VA, HLA Study No. 343-216, 3/13/90); S-3206 (Lot # 70711, 91.9% purity); oral; 0 (corn oil), 0.4, 1.5, 2, 3, 6, or 10 mg a.i. /kg/day in corn oil to 30 female CDF*(F-344)/Cr1BR rats on days 6 to 15 of gestation; **possible adverse effect:** unscheduled deaths in 7 pregnant rats, tremors, ataxia, and convulsions in rats treated at 10 mg/kg/day; decrease in maternal body weight gain (87 % and 70% of control, $P \leq 0.05$) at 6 and 10 mg/kg/day, respectively; microphthalmia noted in one fetus in each dose group (0, .4, 1.5 and 10 mg/kg/day) but was not dose-related; incomplete ossification of the 5th/6th sternebra reported in all dose groups; no evidence of embryotoxicity, fetal toxicity, or teratogenicity was reported at any dose level; maternal NOEL = 3 mg/kg/day (based on tremors, ataxia, convulsions, decreased body weight gain, and unscheduled deaths); developmental NOEL ≥ 10 mg/kg/day (no effects reported at any dose level); study **acceptable** (Leung, 12/28/90).

TERATOLOGY, RABBIT

008, 064; 9839, 91144; "Toxicity of WL-41706: Teratological Studies in Rabbits Given WL-41706 Orally" (Shell Research Limited, London, England, Lab. Report No. FT-51-0006, 8/80); Dutch rabbits; 833; WL-41706 (batch 24, 97% purity); oral by gelatin capsule; 0, 0 (corn oil), 1.5, 3.0, 6.0 mg/kg/day to 20-31 females/dose on days 6-18 of gestation; **no adverse effects indicated;** maternal NOEL = developmental NOEL ≥ 6 mg/kg/day (no effects observed with highest dose tested); no justification of dose levels employed; no in-life observation, food consumption data, animal husbandry, and individual data reported; study **unacceptable** but **possibly upgradeable** with submission of additional data to correct deficiencies as indicated above; (de Vlaming and Gee, 11/4/85; updated Leung, 12/27/90).

**** 065; 91145;** "The Effect of S-3206 on Pregnancy of the New Zealand

White Rabbit" (Huntingdon Research Centre, Ltd., Huntingdon, England, Lab. Report No. FT-51-0134, 11/13/85); 833; S-3206 (batch no. 20514, 92.5% purity); oral gavage; 0 (corn oil), 4, 12, or 36 mg/kg/day to 17-19 females/dose on days 7-19 of gestation; **possible adverse effect:** unscheduled death in 1 pregnant rabbit at high dose; 2 rabbits (including 1 of which is non-pregnant) exhibited shaky movements/trembling at high dose; dose-related increase in the incidence of grooming after dosing; no gross macroscopic changes attributed to treatment were reported; one dam upon autopsy had an interrupted right uterine horn; no treatment-related effects on litter parameters or the incidence of malformations, anomalies, or skeletal variations; maternal NOEL = 12 mg/kg/day (based on shaky movements/trembling); developmental NOEL \geq 36.0 mg/kg/day (no effect at HDT); study **acceptable**; (Leung, 1/2/91).

GENE MUTATION

** 009, 071; 9842, 91152; "Gene Mutation Test of S-3206 in Bacterial System" (Takarazuka Research Center, Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report No. FT-40-0107, 3/19/84; addendum: FT-40-0115, 3/12/84); S-3206 technical (Lot # 20514, 92.5% purity); tested with Salmonella typhimurium strains TA-98, TA-100, TA-1535, TA-1537, TA-1538, Escherichia coli strain WP2uvrA (trp-) with and without activation by PCB (Kanechlor-400)-induced rat liver S9 fraction; duplicate plates; two trials; concentrations of 0(DMSO), 50, 100, 500, 1000, and 5000 ug/plate; 20 minute preincubation period or exposure to S-3206 before plating; 48 hr incubation; positive controls functional; **no adverse effects indicated:** no increase in revertants reported; after initial review, study was found to be **unacceptable** but **possibly upgradeable** with submission of individual data; (de Vlaming and Gee, 10/29/85); study rereviewed with individual plate values subsequently submitted as an addendum; **acceptable**; (Leung, 12/13/90).

009; 9847; "Studies on Mutagenicity of Some Pyrethroids on Salmonella Strains in the Presence of Mouse Hepatic S9 Fractions" (Institute for Biological Science, Hyogo, Japan, Lab. Report No. AT-70-0157, 8/4/77); S-3206 (Lot No. 22018, 97% purity); tested with Salmonella typhimurium strains TA-98, TA-100, TA-1535, TA-1537, TA-1538 with activation by PCB-induced mouse (6 strains) S9 fraction; 3 replicates; 1 trial; (DMSO), 10, 100, or 1000 ug/plate; 48 hr incubation; positive controls were not functional with TA-1537 strain; **no adverse effects indicated:** no increase in revertant colonies reported; individual data not reported; no justification for dose levels and the use of mice rather than rat hepatic S9 fractions; cell survival not measured; study **unacceptable** and **not upgradeable**; (de Vlaming and Gee, 10/28/85; updated Leung, 12/14/90).

009, 070; 9849, 91151; "An Assessment of the Mutagenic Potential

of S-3206 Using an In Vitro Mammalian Cell Test System" (Huntingdon Research Centre, England, Lab. Report No. FT-21-0060, 3/25/82); S-3206 technical (batch No. 01113, 91.4% purity); tested with L5178Y TK +/- cells (3.7.2C) with and without activation by aroclor 1254-induced rat liver S9 fraction; 2 replicates/dose; 1 trial; 3 hour incubation; concentrations of 0 (DMSO), 50.3, 84.5, 141.9, 238.2 without S9 activation, concentrations of 0 (DMSO), 47.5, 75.3, 119.4, 189.2 with S9 activation; positive control functional; **no adverse effects indicated**: no increase in mutation frequency/ 10^6 survivors seen without S9 activation; result with S9 activation equivocal; no repeating or confirming trial; study **unacceptable** and **not upgradeable**; (de Vlaming and Gee, 20/28/85; updated Leung, 12/17/90).

CHROMOSOME EFFECTS

** 009, 073; 9841, 91154; "In Vitro Sister Chromatid Exchanges Test of S-3206 in CHO-K1 Cells with Addendum, Comments and EPA Review" (Biochemistry & Toxicology Laboratory, Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report No. FT-40-0108, 3/19/84); S-3206 technical (Lot # 20514, 92.5% purity); tested in Chinese hamster ovary cells (CHO-K1) with and without activation by PCB-induced rat liver S9 fraction; concentrations 0 (DMSO) and a dose range of 3×10^{-6} to 10^{-4} M; 4 cultures/dose; 2 trials; 2 hr exposure followed by 28 hr incubation period with Brdu; 50 cells/dose scored for sister chromatid exchange; positive controls functional; **no adverse effects indicated**: S-3206 does not induce any SCE in CHO-K1 cells in the presence or absence of S9 activation; study **acceptable**; (Leung, 12/20/90).

009; 9843; "Micronucleus Test of S-3206" (Takarazuka Research Center, Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report No. FT-40-0106, 3/19/84); S-3206 technical (Lot # 20514, 92.5% purity); single i.p.; 0 (corn oil), 50, 100, or 200 mg/kg; high dose group repeated in second experiment; mitomycin C (2 mg/kg, positive control); 6 male ICR mice/dose group; bone marrow samples taken at 24 hrs plus 48 and 72 hrs for 200 mg/kg after dosing; positive control functional; **no adverse effects indicated**: S-3206 does not induce micronuclei in bone marrow erythrocytes of mice; individual data not reported; no justification for using only male animals; study **unacceptable** and **not upgradeable**; (de Vlaming and Gee, 10/29/85; updated Leung, 12/18/90).

009; 9848; "Toxicity Studies with WL-41706: Chromosome Studies on Bone Marrow Cells of Chinese Hamsters After Two Daily Oral Doses of WL-41706" (Shell Research Limited, London, England, Lab. Report No. FT-51-0003, 12/75); WL-41706 (batch # 24, 97% purity); tested in Chinese hamsters; two successive daily oral doses: 0 (DMSO), 10 or 20 mg/kg; cyclophosphamide (100 mg/kg, positive control); 5-6 hamsters/sex/dose; 2 trials; 90 minutes before termination at 8 and 24 hrs after second dose, rats were treated with 0.01 ml of 0.04% Colcemid

solution/g body weight (i.p.); 100 cells analyzed from the bone marrow of each animal; positive control functional; **no adverse effects indicated**: two daily oral doses of WL-41706 did not induce any demonstrable chromosome damage in Chinese hamster bone marrow cells at either sampling time interval; individual data not presented, mitotic index not reported, no justification of dose level, and criteria for scoring not included; study **unacceptable** and **not upgradeable**; (de Vlaming and Gee, 10/28/85; updated Leung, 12/18/90).

** 072; 91153; "In Vitro Chromosomal Aberration Test of S-3206 in Chinese Hamster Ovary Cells (CHO-K1)" (Biochemistry & Toxicology Laboratory, Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report# FT-90-0200, 5/17/89); S-3206 technical (Lot # 20514, 92.4% purity); tested in Chinese Hamster Ovary Cells with and without activation by PCB-induced rat liver S9 fraction; 100 cells from each duplicate/dose scored for chromosomal aberrations; single trial; concentrations 0 (DMSO) and a dose range of 10 - 1000 ug/ml; 2 and 18 to 24 hr exposure with and without S9 activation, respectively; positive control functional; **no adverse effects indicated**: S-3206 did not induce any significant increases in the frequencies of cells with structural aberrations both in the presence or absence metabolic activation; study **acceptable**; (Leung, 12/19/90)

DNA DAMAGE

009; 9846; "Toxicity Studies with WL-41706: Mutagenicity Studies with WL-41706 in the Host-Mediated Assay"(Shell Research Limited, London, England, Lab. Report No. FT-61-0007, 8/80); WL-41706 (batch No. 24, 97% purity); mitotic gene conversion in Saccharomyces cerevisiae strain JD1 after oral dosing of CF male mice with WL-41706 at 0 (DMSO), 10, or 20 mg/kg; ethyl methanesulfonate (EMS, 400 mg/kg); 4 replicates/dose; 3 trials; positive control functional; **no adverse effects indicated**: no increase mitotic gene conversion detected; study **unacceptable** but **possibly upgradeable** with submission of individual data, dose level and animal specie justification, and evidence that the test article is absorbed and reaches peritoneal cavity after oral administration; (de Vlaming and Gee, 10/28/85; updated Leung, 12/13/90).

** 009; 9844; "Autoradiographic Assessment of DNA Repair in Mammalian Cells After Exposure To S-3206 (Fenprothrin)"(Huntingdon Research Centre, Cambridgeshire, England, Lab. Report No. FT-21-0068, 6/16/82); S-3206 technical (Lot # 1113, 91.4% purity); tested with HeLa S3 cells with and without activation by aroclor 1254-induced rat liver S9 fraction; concentrations 0 (DMSO) and a dose range of 200 - 3200 ug/ml; precipitation occurred at \geq 100 ug/ml; 2 replicates; 3 trials; 90 or 180 minute exposure; positive controls in the presence of S9 activation were borderline in increase in number of silver grain; **no**

adverse effects indicated: treatment with S-3206 did not result in any significant increase in unscheduled DNA synthesis by autoradiography; study **acceptable** (de Vlaming and Gee, 10/28/85; updated Leung, 12/21/90)

009; 9850; "Studies on DNA-damaging Capacity of S-3206 with Bacillus subtilis" (Research Dept., Sumitomo Chemical Co., Ltd., Osaka, Japan, Lab. Report No. FT-00-0038, 8/80); S-3206 technical (Lot # 22018, 97% purity); tested with Bacillus subtilis M45 rec⁻ and H17 wild type strains without activation; 4 plates/dose; 2 replicated trials; 24 hr incubation; dose range of 0 - 5000 ug/paper disk; positive control functional; **no adverse effects indicated:** S-3206 did not exhibit any inhibition of growth with either strain; no test or evidence of diffusion of test article in agar; no justification for dose level selection; individual data not reported and growth inhibition of both strains in the presence of metabolic activation not investigated; study **unacceptable and not upgradeable;** (de Vlaming and Gee, 10/28/85; updated Leung, 12/20/90).

NEUROTOXICITY

50489-007; 09836; Acute Delayed Neurotoxicity; 817; Rat; Shell Research Limited, Sittingbourne Research Sittingbourne, Kent, England, Report # TLGR.0041.76, June 1976; WL 41706; 6/sex/dose; 1 dose of 900 ppm in diet (exposure duration not explicitly stated); mortalities- males: 2/6; females: 6/6; observations- males: fine tremors on day 2 after initial exposure, with tremors becoming violent along with erratic jumping behavior in 3/6 by day 12 with one found dead on day 16, another found dead on day 20, with tremors persisting in 4/6 at day 25; females: tremors in all after exposure, with all dead or sacrificed due to morbidity by day 5; necropsy- swelling and disintegration of nerve axons in all with the exception of 1/6 males; **possible adverse effect indicated:** swelling and disintegration of nerve axons; **Reported NOEL=NOAEL < 900 ppm.** Very brief report. Full report needed to determine acceptability of study. (Corlett, 11/15/90)

50489-049; 91129; Acute Delayed Neurotoxicity; 817; Hen; Shell Research Limited, Shell Toxicology Laboratory, Tunstall, England, Report TLGR.0068.77, August 1977; WL 41706; 6 hens/group; 5 successive (unprotected) daily doses of 1 g/kg (dosing regime repeated 3 weeks later); positive control (0.5 ml/kg TOTP); negative control (no treatment); no mortalities; observations- positive control: signs of neurological disturbance beginning by the 16th day becoming progressively worse over the following 9 days with histological examination showing degenerating myelin and swollen axons in the sciatic nerve and degenerating myelin in the spinal cord; experimental

and negative control groups: no signs of neurological disturbance and no histological lesions found; NOEL = NOAEL \geq 1 g/kg; **Supplemental** (a dose of 1 g/kg was used, although the oral LD50 was greater than 1.5 g/kg). (Corlett, 11/14/90)