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
** 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).

**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) > 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 (20-28º) 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 Vlamming 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) > 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 > 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 > 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 due to missing appendices and individual data (de Vlaming and Gee, 11/4/85); study unacceptable but possibly upgradeable with submission of dose analysis; (Leung, 12/28/90).

** 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)/CrI BR 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< 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 > 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. 0111, 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**

09; 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).

09; 9846; "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 (Fenpropathrin)"(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 ≥ 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 > 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)