

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE  
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

Pirimiphos-Methyl

SB 950 # not assigned, Tolerance # 409

November 28,

1988

1. DATA GAP

STATUS

Chronic toxicity, rat:	Data gap, inadequate study, no adverse effect indicated
Chronic toxicity, dog:	No data gap, no adverse effect
Oncogenicity, rat:	Data gap, no study on file
Oncogenicity, mouse:	Data gap, inadequate study, no adverse effect indicated
Reproduction, rat:	Data gap, inadequate studies, possible adverse effect indicated
Teratology, rat:	Data gap, inadequate study, no adverse effect indicated
Teratology, rabbit:	Data gap, inadequate study, no adverse effect indicated
Gene mutation:	Data gap, no study on file
Chromosome effects:	Data gap, inadequate studies, no adverse effect indicated
DNA damage:	Data gap, inadequate study, no adverse effect indicated
Neurotoxicity:	Data gap, inadequate studies, possible adverse effect indicated

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Toxicology one-liners are attached.

\*\* indicates an acceptable study.

**Bold face** indicates a possible adverse effect.

File name: T881128

Toxicology summary prepared by J.Gee.

## II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

### Chronic Toxicity, Rat

005 005807, "Pirimiphos-Methyl (PP 511): 2-year Feeding Study in the Rat", (ICI Limited, Report # HO/IH/P/113, June 1974), Pirimiphos-Methyl, no purity stated, fed in the diet for two years at 0, 10, 50, or 300 ppm with 48/sex/group. **No adverse effect** reported. Depression of brain (15%-30%), plasma (20%-83%), and RBC (7%-38%) ChE at 50 and 300 ppm. NOEL = 10 ppm. **Unacceptable**, possibly upgradeable (need: dietary analysis, individual animal data, urinalysis information, brain and testes weights, bone marrow examinations, serum chemistry and enzymes). (Carlisle 4/28/86)

### Chronic Toxicity, Dog

\*\*005 005808, "PP 511 Oral Toxicity Study in Beagle Dogs (Repeated Daily Dosage for Two Years)", (Huntingdon Research Centre, report # 5438/72/834, 5/8/73), Pirimiphos-Methyl, 97% purity, administered in gelatin capsules daily for 2 years at 0 (undosed control), 0.5, 2.0, and 10.0 mg/kg/day with 4/sex/group. Slight inhibition of brain (19%) and plasma (25%) ChE at 0.5 mg/kg/day. Soft stools and inhibition of brain (22%), plasma (33%), and RBC (50%) ChE at 2.0 mg/kg/day. Transient decreased bodyweight gain, soft stools, increased liver weight, and inhibition of brain (56%), plasma (34%), and RBC (83%) ChE at 10.0 mg/kg/day. **No adverse effect**. NOEL = 0.5 mg/kg/day (clinical signs, ChE effects). **Acceptable**. (Carlisle 4/24/86)

### Oncogenicity, Rat

See "Chronic Toxicity, Rat" above.

### Oncogenicity, Mouse

003 001805, 001806, "Long-Term Feeding of Pirimiphos-Methyl (PP 511) in Mice (Final Report 0-80 Weeks)", (Huntingdon Research Centre, report # ICI 34/7658, 7/15/76), Pirimiphos-Methyl, 97.8% purity, fed in the diet for 80 weeks at 0, 5, 250, or 500 (initially treated at 300 ppm and increased by weekly increments of 50 ppm to 500) ppm with 52/sex/group and satellite groups of 12/sex for ChE investigations at all levels except 250 ppm. Plasma ChE inhibition at 5 (10%-35%) and 500 (78%-86%) ppm; RBC ChE inhibition at 5 (25%-30%) and 500 (70%-86%) ppm. No adverse effect reported. NOEL = 5 ppm (ChE inhibition). **Unacceptable**, no hematology results and inadequate histopathology findings. (Carlisle 5/8/86)

### Reproduction, Rat

**004 001816**, 001817, "Effect of PP511 on Reproductive Function of Multiple Generations in the Rat, Final Report", (Huntingdon Research Centre, report # 5457/72/853, 12/17/72), Pirimiphos-Methyl, no purity stated, fed in the diet through 3 generations (through 4 generations at 20 ppm) at 0, 20, and 200 ppm with 12 males and 24 females/group. **Adverse** effects: decreased mating performance and pregnancy rate reported at 20 and 200 ppm. Reproductive NOEL < 20 ppm; parental NOEL  $\geq$  200 ppm. **Unacceptable**, not upgradeable (too few dose groups; no histopathology data on vagina, seminal vesicles or prostate). (Carlisle 5/6/86)

004 001818, "Effect of Pirimiphos-Methyl (PP 511) on Reproductive Function of Multiple Generations in the Rat", (Huntingdon Research Centre, report # ICI 63/76534, 8/31/76), Pirimiphos-Methyl, no purity stated, fed in the diet over 3 generations at 0, 5, 10, and 100 ppm with 20 rats/sex/group. ChE inhibition in Fo generation: plasma (14%-47%); RBC (17%-40%) reported at 100 ppm. No reproductive effects indicated. **No adverse effect** reported. Reproductive NOEL  $\geq$  100 ppm; parental NOEL = 10 ppm (ChE inhibition). Unacceptable, possibly upgradeable with submission of histopathologic findings on vagina, uterus, ovaries, testes, epididymis, seminal vesicles, and prostate of adult breeders. (Carlisle 5/7/86)

Note: Although both studies are unacceptable at this time, possible adverse effects are indicated for the category.

#### Teratology, Rat

005 005803, "Pirimiphos-Methyl (PP 511): Teratological Studies in the Rat", (ICI Limited, report-# HO/IH/P/59, September 1972), Pirimiphos-Methyl, 95% purity, fed in the diet on days I through 20 of gestation at 0, 10, and 200 ppm nominal with 18 to 21 inseminated females/group. High incidence of hydronephrosis in fetuses (reported to be within normal limits for Alderly Park rats) reported at 10 and 200 ppm. No adverse effect reported. **Unacceptable**, possibly upgradeable with submission of full study. (Carlisle 5/5/86)

Note. Letter 409-007 from ICI to EPA dated 9/19/84 indicated a new rat teratology study would be conducted.

#### Teratology, Rabbit

004 001812, "Pirimiphos-Methyl (PP511): Teratogenicity Study in the Rabbit", (ICT Limited, report # HO/CTL/P/119B, July 1974), Pirimiphos-Methyl, 93.1% purity, administered in gelatin capsules on days 1 through 28 of gestation at 0 (corn oil), 1, and 16 mg/kg/day with 16-17 mated females/group. No evidence of developmental toxicity reported. No adverse effect indicated. Maternal and fetotoxic NOEL  $\geq$  16 mg/kg/day. ChE NOEL = 1 mg/kg/day. Unacceptable, not upgradeable (too few dose levels, too few fetuses examined, no soft tissue data). (Carlisle 5/6/86)

#### Gene Mutation

No study on file.

#### Chromosome Effects

005 005802, "Cytogenetic Study in Rats of Pirimiphos-Methyl", (Inveresk Research International, report # 1603, May 1980), Pirimiphos-methyl, batch Y0146/003/002 and Y0146/013/001, 89.9% purity, 10 males were given 0 (corn oil), 32, 102 or 320 mg/kg by oral gavage once or five times. Sacrificed at 6 and 24 hours after single dose and 6 hours after 5th dose. No increase in aberration. **Unacceptable** (use of males only without justification). (Gee 4/22/86).

004 001814, "Dominant Lethal Study in Mice of Pirimiphos-Methyl", (Inveresk Research International, report # 289, 6/20/75), Pirimiphos-Methyl, no purity stated, 0 (corn oil), 15, 80 or 150 mg/kg given orally on 5 consecutive days to 15 male CD-1 mice (30 for controls). Mated 1 male:2 females over 8 weekly intervals. No dominant lethal effect. **Unacceptable**, upgradeable (characterization of test article, evidence that pirimiphos-methyl reaches germinal cells). (Gee 4/22/86)

#### DNA Damage

005 005804, "An Examination of Pirimiphos-Methyl using the Mammalian Cell Transformation Assay", (Imperial Chemical Industries PLC, Central Toxicology Laboratory, report # CTL/P/827, 2/14/83), Pirimiphos-Methyl, no purity stated, BHK21/C13 exposed with S9 (Aroclor 1254-induced) rat liver fraction for 3 hours to 0 (DMSO), 0.025, 0.25, 2.5, 25, and 250  $\mu$ g/ml. Acrylonitrile as positive control. **Unacceptable**, not upgradeable (no -S9 cultures, only 3 hour exposure, too few plates/concentration). (Gee 4/22/86)

#### Neurotoxicity

**006 025251**, "The Acute Oral Toxicity (LD50) and Neurotoxic Effects of Pirimiphos-Methyl on the Domestic Hen", (Huntingdon Research Centre, report # ICI/303NT/80457, 6/20/88), Pirimiphos-Methyl, PP511, 96.7% purity, single dose by gavage at 0 (corn oil), 26, 51, and 102 mg/kg with protection (PAM and atropine), TOCP positive control, with 10 hens/group (2 groups at 102 mg/kg). Acute toxicity reported at 26, 51, and 102 mg/kg. 3 deaths at 51 mg/kg; 4/group and 5/group, respectively, at 102 mg/kg. **Adverse effects:** delayed but apparently reversible neurotoxicity reported. **Unacceptable**, possibly upgradeable (individual clinical observations and histopathology are needed). (Carlisle 4/17/86)

004 001827, "Examination of Pirimiphos Methyl for Neurotoxicity in the Domestic Hen", (Huntingdon Research Centre, report # ICI/49/75220, 8/11/75), Pirimiphos-Methyl, no purity stated, single dose by oral intubation at 0 (arachis oil), 20, 30, 40, 50, and 60 mg/kg with 5 hens/group. TOCP as positive control. Groups at 50 and 60 mg/kg were redosed with protection (atropine and PAM) at 21 days. LD50 reported: 78.9 mg/kg. # deaths/# treated after initial dose: 1/5 at 40 mg/kg, 1/5 at 50 mg/kg, and 3/15 at 60 mg/kg. # deaths/# treated after redosing at day 21: 1/5 at 50 mg/kg and 2 (+ 1 hen added at day 21)/5 at 60 mg/kg. Slight ataxia reported in 1 hen at 50 mg/kg. Slight to severe ataxia reported in all hens receiving TOCP. Histopathology revealed minimal neuropathological changes (perivascular cuffing with mononuclear cells and focal aggregates of glial cells) in all pirimiphosmethyl treated hens. The changes were reported as spontaneous in origin and not treatment related. Unacceptable, not upgradeable (inadequate dose levels, insufficient numbers/group for histopathology). (Green 11/10/88, Gee 11/18/88)