

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY  
DEPARTMENT OF PESTICIDE REGULATION  
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

Temephos

Chemical Code # 1, Tolerance # 170  
SB 950 # 892

11/9/99

I. DATA GAP STATUS

Combined, rat:	Inadequate study; no adverse effect indicated
Chronic toxicity, dog:	No study on file
Oncogenicity, mouse:	No study on file
Reproduction, rat:	Inadequate study; no adverse effect indicated
Teratology, rat:	No study on file
Teratology, rabbit:	Inadequate study; no adverse effect indicated
Gene mutation:	Inadequate study; no adverse effect indicated
Chromosome effects:	No data gap; no adverse effect indicated
DNA damage:	No data gap; no adverse effect indicated
Neurotoxicity:	No data gap; no adverse effect indicated.

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Toxicology one-liners are attached.

All record numbers through 60127 were examined.

\*\* indicates an acceptable study.

Bold face indicates a possible adverse effect.

## indicates a study on file but not yet reviewed.

File name: T991109

Tom Moore, 11/9/99

## II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

### COMBINED, RAT

011,012; 37478, 37479, 37480; "Two Year Chronic Toxicity and Carcinogenesis Study of Temephos in the Rat"; (P.C. Underwood; Pharmacopathics Research Laboratories, Inc., Laurel, MD; Report No. 7354; 10/4/77); Sixty Sprague-Dawley rats/sex/group were dosed with 0, 10, 100 or 300 ppm of temephos technical (purity: 93.5%) in the diet for 24 months. The animals in the treated groups were exposed *in utero* from gestation day 12 through parturition to 100 ppm of the test material. At the time of weaning the pups were randomly allocated to the three treatment groups and the treatment initiated. The control group was derived from a separate group of animals. Survival was not affected by the treatment. The mean body weights for the high dose males was 7% less than that of the controls at the conclusion of the study. Otherwise, no other apparent treatment-related effects were noted. There were no treatment-related effects upon the parameters evaluated for hematology, clinical chemistry or urinalysis. Although mean relative liver weights were greater for animals in the treated groups, there was no apparent dose-related effect nor accompanying histopathological or clinical chemical evidence of injury. **No adverse effects indicated. NOEL:** not determinable; **Study unacceptable**, not upgradeable (lack of test diet analysis, ophthalmology, dose level justification, valid control group, and rationale for exposing animals *in utero* to 100 ppm of the test material, inadequate number of animals used in hematology and serum chemistry). (Moore, 10/13/99)

### CHRONIC TOXICITY, RAT

See above.

### CHRONIC TOXICITY, DOG

Study not submitted.

### ONCOGENICITY, RAT

See above.

### ONCOGENICITY, MOUSE

Study not submitted.

### REPRODUCTION, RAT

013; 37481; "Abate Mosquito Larvicide: Successive Generation Studies in Rats"; (M. Mcnerney, W.E. Ribelin and G.J. Levinskas; American Cyanamid Company, Central Medical Department, Environmental Health Laboratory, Wayne, NJ; Report No. 68-9; 1/26/68); Twenty four female and 12 male rats/group of the P generation were treated in the diet with 0, 25, or 125 ppm of Abate Mosquito Larvicide, technical (purity: 87.1%) for 8 weeks prior to mating, up to 20 days during mating, followed by 3 weeks each of gestation and lactation. Sixteen animals/sex/group in the F1 generation and F2 generations were fed the diet at least 8 weeks prior to mating, up to 20 days during mating, followed by 3 weeks each of gestation and lactation. A second mating of the F2 generation was performed approximately 10 to 11 weeks after the first mating with treatment during the 3 weeks each of gestation and lactation. No treatment-related signs for the adults were reported. The mean body weights for the females and the males in the F1 generation and the females in the F2 generation of the 125 ppm treatment group were lower at the time of mating than those of the control animals. Although the viability index for the 125 ppm F3 generation pups in the first mating was lower than that for the control group, no significant treatment-related effects were noted for the reproductive parameters. Mean body weights for the 125 ppm pups of the F1, F2 and F3, 1<sup>st</sup> mating, at the time of weaning were less than those of the control pups. **No adverse effects indicated. Parental NOEL:** not determinable; **Reproductive NOEL:** not

determinable, **Developmental NOEL**: not determinable. **Study unacceptable**, not upgradeable (lack of test diet and statistical analysis, incomplete necropsy and histopathology, and inadequate number of animals, only two dose groups). (Moore, 9/28/99)

#### TERATOLOGY, RAT

Study not submitted.

#### TERATOLOGY, RABBIT

014; 37482; "Teratology Study in Rabbits: Abate Technical"; (R.P. Beliles; Litton Bionetics, Inc., Kensington, MD; Project No. 20740-B; 6/6/78); At least 14 mated New Zealand White female rabbits/group were treated orally by gavage with 0, 3, 10, or 30 mg/kg/day of Abate Technical (purity: 90.4%) from gestation day 6 through 18. No apparent treatment-related mortality resulted from the dosing. No clinical observations were noted in the study. There were no treatment-related effects on maternal body weights. Maternal mean kidney weight was lower for the 30 mg/kg/day group than that of the control ( $p < 0.05$ ). There was an increased percentage of fetuses with external, visceral or unusual skeletal variations (0: 4.82, 3: 5.05, 10: 13.33, 30: 10.29%). However, the numbers of litters/group with abnormal fetuses was 4 for all of the groups, indicating that the affected fetuses were concentrated within the same litters. **No adverse effect indicated. Reported Maternal NOEL**: 10 mg/kg/day (based upon lower mean kidney weights of the 30 mg/kg/day females), **Reported Developmental NOEL**: 30 mg/kg/day (HTD) ; **Study unacceptable**, but possibly upgradeable with dosing solution analysis. (Moore, 9/23/99)

#### GENE MUTATION

015; 37483; "Mutagenicity Testing of Technical Abate Temephos in the Ames Bacterial Test"; (J.S. Allen; American Cyanamid Company, Agricultural Division, Research and Development Department, Princeton, NJ; Project No. 0-796; 4/13/78); *S. typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537 and *E. coli* WP-2 uvrA<sup>-</sup> were treated by the plate incorporation method for 48 hours at 37° C with Abate Technical (purity: 90.4%, Batch #599) at concentrations ranging from 10 to 1000 ug/plate. In addition, the same strains were exposed to 1000 ug/plate of the test material by the disc method under the same conditions of incubation. One plate/treatment level for one trial was performed. Each treatment level was incubated under conditions of "activation" and "non-activation". An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. There was no treatment-related increase in the incidence of reverse mutation. **No adverse effect indicated. Study unacceptable**, not upgradeable (lack of dose level justification and/or inadequate dose level selection, single plate per concentration, inappropriate positive controls  $\pm$  S9 ). (Moore, 9/29/99)

015; 37484; "Mutagenicity Evaluation of Abate: Quantitative Suspension, Mutagenicity Assay"; (D.R. Jagannath; Litton Bionetics, Inc., Kensington, MD; Project No. 20988; 4/6/79); *S. typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 were preincubated with concentrations of Abate (purity not identified) which ranged from that which resulted in 50% cell survival to 1/8 of that concentration for 1 hour at 37° C under conditions of "activation" and "non-activation" by the method of plate incorporation. At the conclusion of the preincubation period, diluted cell suspensions and undiluted samples (5 plates/treatment level) were incubated for an additional 48 hours at 37° C. The S9 fraction used for "activation" was derived from the liver homogenate of rats pretreated with Aroclor-1254. No treatment-related increase in the incidence of reverse mutation was noted. No adverse effect indicated. **Study unacceptable**, not upgradeable (identification of test material is incomplete). (Moore, 10/1/99)

#### CHROMOSOME EFFECTS

\*\* 020; 60126; "Test for Chemical Induction of Chromosomal Aberration using Monolayer Cultures of

Chinese Hamster Ovary (CHO) Cells with and without Metabolic Activation"; (A. Thilagar, *et. al.*; Sitek Research Laboratories, Rockville, MD; Study No. 0018-3100; 2/28/86); Chinese hamster ovary cells (CHO, CCL 61) were treated with AC 52,160 (purity: 94.7%) at concentrations which ranged from 0.05 to 7.5 ul/ml under conditions of activation and non-activation at 37° C. In the activated assay, the cells were treated for 2 hours with test material and then incubated further for 8 (1st harvest) or 18 hours (2nd harvest). For the non-activated samples, the cells were exposed to the test material for 10 (1st harvest) or 20 hours (2nd harvest). All of the samples were incubated for an additional 2 hours with Colcemid and fixed and prepared for evaluation. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. Two replications were performed for each treatment level. There was no apparent treatment-related increase in chromosomal aberrations. **No adverse effect indicated. Study acceptable.** (Moore, 10/6/99)

#### DNA DAMAGE

\*\* 020; 60127; "Rat Hepatocyte Primary Culture/DNA Repair Test"; (T.R. Barfknecht; Pharmakon Research International, Inc., Waverly, PA; Report No. PH 311-AC-004-85; 1/13/86); Primary rat hepatocyte cultures were exposed to AC 52,160 (purity: 94.7%) at concentrations ranging from 166 to 5000 µg/ml for 18 to 20 hours at 37°C. A single trial was performed with triplicate cultures/treatment level. There was no treatment-related increase in the incidence of unscheduled DNA synthesis. **No adverse effect indicated. Study acceptable.** (Moore, 10/7/99)

#### NEUROTOXICITY

\*\* 016; 37485; "Examination of Temephos for Neurotoxicity in the Domestic Hen"; (D.B. Ross *et. al.*; Huntingdon Research Centre, Huntingdon, Cambridgeshire, England; Report No. CYD/202/75236; 4/1/76); Six adult hens/group were orally dosed by gavage with 0, 227, 455, 823, 1137, 1422, and 1705 mg/kg of Temephos Technical (purity: 99.9%) in a determination of the LD50 value. Six hens were also dosed with 450 mg/kg of TOCP as a positive control. The following mortality resulted from the treatment: 0 (1/6), 227 (1/6), 455 (3/6), 823 (4/6), 1137 (5/6), 1422 (4/6), and 1705 (4/6). All of the TOCP treated hens survived the treatment, but five of the birds exhibited signs of ataxia by day 16. These observations were confirmed by histological examination of the brain, spinal cord, and sciatic nerve (chromatolysis of neurons, swollen and disrupted axons, and fiber degeneration in the peripheral nerves). After 21 days of observation, the 5 birds in the 227 mg/kg group and the 3 birds in the 455 mg/kg group received an additional dose of 227 and 455 mg/kg and observed for another 21 days. Another group of 6 hens were treated with 455 mg/kg. At the time of this second dosing, all of the birds were treated with atropine (6.5 mg/kg) and PAM (43 mg/kg). Among the birds being dosed for a second time, one bird each died in the 227 and 455 mg/kg groups. In the second 455 mg/kg treatment group, 3 hens died. After 21 days of observation, the brain, spinal cord and sciatic nerves of the 3 surviving birds were examined histologically. In the initial portion of the study, the LD50 (95% confidence limits) value was determined to be 579 (287 to 1137) mg/kg. None of the temephos treated animals displayed signs of ataxia. The histological examinations did not reveal any neuronal degeneration. **No adverse effect indicated. Study acceptable.** (Moore, 10/4/99)

170-016; 37486; "Abate Mosquito Larvicide: Demyelination Studies in White Leghorn Hens"; (author not identified; American Cyanamid Company, Central Laboratory Department, Environmental Health Laboratory; Report No. 67-25; 2/14/67); In the initial study, three hens/group were dosed orally with single doses of 41, 82, 163, or 326 mg/kg of AbateMosquito Larvicide (technical) (purity: 87.1%). One hen died in the 82 mg/kg group and all 3 hens died in the 326 mg/kg group. An LD50 value of 183 mg/kg was calculated from these data. In the second study, 8 hens/group were fed diets containing 230, 460, or 920 ppm of the test material for 30 days. An additional 6 hens received 4000 ppm of TOCP in the diet for the same time period. After 30 days, 2 birds each from the control and TOCP group and 4 birds from the 920 ppm group were euthanized and the brain, spinal cord and sciatic nerves were examined histologically. The remaining birds in the 920 ppm group received the basal laboratory diet for another 4 weeks. The surviving hens in the 230 and 460 ppm groups were euthanized one week after

receiving the control diet. One hen died in the 460 ppm group after 23 days of treatment. Four of the TOCP treated birds died, the first approximately 4 weeks after initiation of the study. Death was preceded by muscular weakness, paralysis and severe malnutrition. The histological examination of the TOCP treated hens revealed focal myelin loss in the medullary substance of the cerebellar hemispheres, in the fasciculus gracilis and the cuneatus of the spinal cord and in the peripheral nerve. All of the Abate-treated hens lost weight during the treatment period, possibly due to the lack of palatability of the test material. Histological examination of the hens did not reveal any treatment-related lesions in the nervous system. The concentration of the test material in the dietary preparations and the food consumption of the hens were not determined, thereby not permitting an adequate determination of the actual test material consumed by the test animals. **No adverse effect indicated. Study supplemental** (not a guideline study). (Moore, 10/4/99)

### SUBCHRONIC STUDIES

170-001; 6257; "CL 52,160: Ninety-Day Feeding to Albino Rats; (G.J. Levinskas; American Cyanamid Company, Central Medical Department, Environmental Health Laboratory, Wayne, NJ; Report No. 65-18; 3/9/65); Forty five rats/sex/group received 2, 6, or 18 ppm of CL 52,160 Technical (purity: 96.4%) in their diet for up to 13 weeks. Another group of 45 animals/sex were treated with 350 ppm of the test material for 12 weeks. Sixty five animals/sex were included as a control group. Seven control rats/sex and 4 animals/sex/treatment group (except for the 350 ppm group) were sacrificed at 1, 3, 5, 9 and 13 weeks of study and erythrocyte, plasma and brain cholinesterase activities were determined. For the 350 ppm group, 4 animals/sex were sacrificed after 12 weeks of treatment for cholinesterase activity determinations. At the conclusion of the treatment period, 15 control animals/sex and 10 animals/sex/treatment group were permitted to recover for up to 4 weeks. One control male, one 6 ppm female and one 18 ppm female died during the study. No treatment-related signs were noted. The mean weight gain for both the males and females in the 350 ppm group was less with the difference being significant for the females ( $p<0.05$ ). Erythrocyte cholinesterase activity was most affected by the treatment with the mean activity less than 80% of the control values for the 18 ppm treatment group at various time points during the study ( $p<0.05$ ). Only at one time point for the 6 ppm group (13 weeks) was the activity level less than 80% of the control group. The activity levels for the animals in the 18 ppm group had largely recovered by the end of the 4 week recovery period. The plasma cholinesterase activity level was significantly reduced only for the 350 ppm treatment group. Brain cholinesterase activity levels were significantly reduced for the 18 ppm group during the first five weeks of the study. However, the most reduction in the activity level was 81% of the control value. For the 350 ppm treatment group, mean brain cholinesterase activity levels were 23 and 22% of control values for males and females respectively. The mean relative liver weight was significantly reduced for the males in the 350 ppm group ( $p<0.05$ ). Otherwise, no apparent treatment-related effects were noted in the necropsy and histopathological examinations. **Adverse effect:** brain cholinesterase inhibition. Reported **NOEL (M/F):** 6 ppm (based upon significant brain cholinesterase inhibition noted for the 18 ppm treatment group); **Study unacceptable**, not upgradeable (concentration of the active ingredient in the dietary preparations not analyzed, no hematology, clinical chemistry or ophthalmology performed.). (Moore, 9/10/99)

170-001; 6256; "CL 52,160: Ninety-Day Repeated Feeding to Dogs"; (E.B. Hutchison; American Cyanamid Company, Central Medical Department, Environmental Health Laboratory, Wayne, NJ; Report No. 65-19; 3/19/65); Two beagle dogs/sex/group (unless otherwise noted) received 0, 2, 6, or 18 ppm of CL 52,160 Technical (purity: 96.4%) in the diet for 13 weeks. One male and 3 females were included in the 18 ppm treatment group. The animals remained on study for an additional two weeks after the termination of the dosing. An additional group of two animals/sex were dosed for 15 days with 700 ppm of the test material, followed by an additional 10 weeks of treatment with 500 ppm in the diet. Erythrocyte and plasma cholinesterase activities were measured prior to study initiation and on weeks 1, 3, 5, 9, and 13 (week 12 for animals in the high dose group and 2 weeks after the animals returned to

basal diet). Treatment with 700 ppm resulted in the appearance of cholinergic signs such that the treatment level was reduced to 500 ppm after two weeks. The cholinergic signs were still evident but less severe in presentation. Brain cholinesterase values were determined for the high dose group after 12 weeks of treatment. Although no control values for brain cholinesterase activity were determined, the brain cholinesterase activity in the treated animals was reported as markedly inhibited. No treatment-related lesions were noted for the 700/500 ppm group. **Adverse effect:** significant brain cholinesterase inhibition; Reported **NOEL (M/F):** 18 ppm (based upon the treatment-related effects noted for the 700/500 group); **Study unacceptable**, not upgradeable (concentration of the active ingredient in the dosing preparations not analyzed, fewer than the recommended number of animals/sex/group, hematology, clinical chemistry and ophthalmology not performed, histopathology on high dose only). (Moore, 9/13/99)

170-001; 6258; "CL 52,160: Three Week Dermal Applications to Rats"; (R.G. Esposito; American Cyanamid Company, Central Medical Department, Environmental Health Laboratory, Wayne, NJ; Report No. 64-123; 11/2/64); The skin of ten rats/sex/group was treated with 0, 12, or 60 mg/kg/day of CL 52,160 for 15 days over a 3 week period. The dosing material was prepared by diluting the CL 52,160 (a.i.: 43%) formulation with water to produce final concentrations of 1.2 and 6.0% of CL52,160.

A dosing volume of 1.0 ml/kg was applied to the skin. The skin of 5 rats/sex/group was abraded prior to application. The skin of the remaining animals was intact. All of the animals survived the treatment. No treatment-related signs were noted. Mean body weight gain for the males in the 60 mg/kg/day group was significantly less than that of the controls ( $p<0.05$ ) with food consumption significantly reduced for the males with intact skin in this group ( $p<0.05$ ). The mean relative liver weights for the 12 mg/kg/day males and the 60 mg/kg/day females were significantly increased ( $p<0.05$ ). Although the livers of the high dose females demonstrated a mild diffuse fatty change, examination of the control females revealed a similar condition. No other potential treatment-related lesions were noted. **No adverse effect indicated.** **NOEL: not determinable.** **Study unacceptable**, not upgradeable (analysis of the active ingredient in the dosing material was not performed). (Moore, 9/9/99)