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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: RfD/Peer Review Report of Fenthion [O,O-Dimethyl-O-[3-methyl-4-(methylthio) phenyl] phosphorothioate]

CASRN: 55-38-9
EPA Chem. Code: 053301
Caswell No.: 456F

FROM: George Z. Ghali, Ph.D. G. Ghali
Manager, RfD/QA Peer Review Committee
Health Effects Division (7509C)

THROUGH: William Burnam
Chairman, RfD/QA Peer Review Committee
Health Effects Division (7509C)

TO: George LaRocca, PM 13
Insecticide-Rodenticide Branch
Registration Division (7505C)

Chief, Reregistration Branch
Special Review and Reregistration Division (7508W)

The Health Effects Division-RfD/Peer Review Committee met on February 23 and again on October 5, 1995 to discuss and evaluate the existing and/or recently submitted toxicology data in support of Fenthion reregistration and to reassess the Reference Dose (RfD) for this chemical. The Committee reconvened on December 7, 1995 to further discuss and address the carcinogenicity issue and to classify the chemical.

In the meeting of February 23, 1995, material available for review consisted of data evaluation records (DERs) for two chronic toxicity/carcinogenicity studies in rats **(83-5 or 83-1a and 83-2a)** two carcinogenicity studies in mice **(83-2b)**, two chronic (one-year) feeding toxicity studies in dogs **(83-1b)**, two multi-generation reproductive toxicity studies in rats **(83-4)**, developmental toxicity studies in rats and rabbits **(83-3a and -3b)**, a 90-day delayed neurotoxicity study in hens **(82-5)**, acute delayed neurotoxicity studies in hens **(81-75)**, a special neurotoxicity study in rats (non-guideline), and a battery of mutagenicity studies **(84-2)**.

In the meeting of October 5, 1995, the Committee discussed two special studies; 1) a plasma cholinesterase (ChE) and red blood cell (RBC) acetylcholinesterase (AChe) inhibition study in human subjects, and 2) a plasma ChE and RBC AChe inhibition study in monkeys. An additional meeting on December 7, 1995 was held to discuss the carcinogenicity issues related to Fenthion.

A. Chronic and Subchronic Toxicity:

The Committee considered the chronic toxicity phase of the rat study (83-1a, MRID No. 41743101) to be acceptable as Core-minimum data, and the data evaluation record for this study (HED Doc. No. 009870) to be adequate. The doses below differ from the original DER due to an error in conversion. The DER has been corrected.

The no-observable effect level (NOEL) for inhibition of plasma ChE, RBC and brain AChE was not established. At 5 ppm (0.2 and 0.3 mg/kg/day for males and females, respectively), the lowest dose level tested, there was 31-41% (in males) and 7-27% (in females) inhibition of plasma ChE throughout the study. There was 7-18% (in both sexes) inhibition of the RBC AChE throughout the study; and 13-14% inhibition of brain AChE (in males) at termination.

Pathological effects including vacuolation were noted in the epididymis and the NOEL and lowest observable effect level (LOEL) were 5 and 20 ppm (0.2 and 0.8 mg/kg/day). Pathological, ophthalmoscopic and electroretinographic evaluation of the eye and/or the optic nerve indicated that Fenthion affected the rat visual system. Females were more susceptible than males and this type of lesion only occurred at doses higher than the LOEL for cholinesterase inhibition. The NOEL and LOEL for effects on the visual system were considered in females to be 5.0 and 20 ppm (0.3 and 1.3 mg/kg/day) and in males to be 20 and 100 ppm (0.8 and 5.2 mg/kg/day).

The Committee considered the one-year chronic toxicity study in dogs (83-1b, MRID No. 41632801, 42901402) to be acceptable and the data evaluation record (009295, 010725) to be adequate. The NOEL for plasma ChE inhibition was 2 ppm (0.056 mg/kg/day in both sexes). Reduction of plasma ChE (31-41%) and RBC AChE (15% males and 3% females) was observed at 10 ppm (0.26 mg/kg/day for both sexes). Reduction of plasma ChE (50-77%), RBC AChE (53-54% in both sexes) and brain AChE (30% but not significant in males, and 44% in females, $p < 0.05$ in females) was observed at 50 ppm (1.23 mg/kg/day in males and 1.18 mg/kg/day in females) at study termination at one year.

The older chronic toxicity studies in rats and dogs (MRID No. 00147478; 00132341) were considered unacceptable and the data evaluation record (HED Doc No. 004239) to be inadequate based on current standards.

In the mouse study (MRID No. 41869201, 42759701, 42901403, HED Doc. No. 009536, 010324, 010725), plasma ChE was inhibited in males at 0.03 (threshold) and in females at 0.47 mg/kg/day. The NOEL in females was 0.03 mg/kg/day but < 0.03 mg/kg/day in males. Brain AChE was inhibited at 1.95 mg/kg/day in males and at 0.47 mg/kg/day in females. Thus, the NOEL was 0.4 and 0.03 mg/kg/day in male and female brain AChE respectively. RBC AChE was inhibited at 9.42 in males and 10.23 mg/kg/day in females and the NOEL was 1.95 and 2.25 mg/kg/day for males and females.

In the meeting of February 23, 1995, the Committee requested that data evaluation records for existing studies on the effect of Fenthion on cholinesterase activity in monkey (MRID No. 00147245, HED Doc. No. 011768) and human (MRID No. 00147246, HED Doc. No. 011768) be submitted to the Committee for evaluation. In the meeting of October 5, 1995, the Committee discussed the monkey and human studies and concluded the following:

1) Monkey study: plasma ChE was intermittently inhibited at 0.02 mg/kg/day (maximum inhibition level 67% in the first six months, especially in females) such that this level was deemed to be a threshold effect level. Progressively more consistent inhibition was observed at 0.07 and 0.2 mg/kg/day. **The threshold NOEL/LOEL for plasma ChE was 0.02 mg/kg/day.** RBC AChE was noted to have a some for inhibition at 0.07 mg/kg/day (frequent inhibition at this level up to 39% for the first three months of the study). More consistent RBC AChE inhibition was noted at 0.2 mg/kg/day. The NOEL and LOEL for the RBC AChE inhibition were 0.02 and 0.07 mg/kg/day. No inhibition of brain AChE and no clinical signs or body weight effects were noted.

2) Human study (male volunteers only): plasma ChE was considered to be inhibited relative to pretest values approximately 5% at 0.02 mg/kg/day and 15% at 0.07 mg/kg/day whereas the control group was actually increased. The 0.02 mg/kg/day dose group was considered to be a threshold for inhibition since, at least, some statistical tests were reported by the study author were significant compared to the control group. RBC AChE was not considered to be inhibited at any dose and there were no changes in clinical observations, chemistry, hematology or urinalysis. **The threshold NOEL/LOEL for plasma ChE inhibition in humans (only males tested) was considered to be 0.02 and 0.07 mg/kg/day** with 0.07 mg/kg/day considered a definitive effect level.

The Committee agreed with the reviewer's evaluation and interpretation of the parameters examined in these studies and recommended no revisions to the data evaluation records as presented.

B. Carcinogenicity:

The Committee considered the carcinogenicity phases of the combined chronic toxicity/carcinogenicity studies in rats (83-2a, MRID No. 41743101, 4269902) and mice (83-2b, MRID No. 41869201, 42759701, 42901403) to be acceptable.

The highest dose levels tested in both the rat (100 ppm) and mouse (25 ppm) studies were considered to be adequate for carcinogenicity testing based on reduction observed in plasma ChE and RBC and brain AChE.

In mice, the increases in hepatocellular adenomas and carcinomas did not appear to be statistically significant or dose-related in either males or females, and were below the average for historical control incidence for males. In rats, the DER stated that "no evidence of carcinogenicity" was observed.

After examination of the tumor summary tables from the study reports, at the meeting on December 7, 1995, the Committee concluded that the chemical did not alter the spontaneous tumor profile in rats and that the total liver tumors observed in male mice did not attain a statistically significant level for trend but was statistically significant in the pairwise comparison with the concurrent control only at 5.0 ppm (mid-high dose level) and not at 25.0 ppm (the highest dose level tested).

The Committee, therefore, recommended that the Fenthion be classified as a **"Group E"**, i.e. the chemical is **not likely** to be carcinogenic to humans via relevant routes of exposure.

This weight of the evidence judgment is largely based on the absence of significant tumor increases in two adequate rodent carcinogenicity studies. It should be noted, however, that designation of an agent as being in Group E is based on the available evidence and should not be interpreted as a definitive conclusion that the agent will not be a carcinogen under any circumstances.

C. Reproductive and Developmental Toxicity:

The Committee considered the 2-generation reproduction toxicity study in rats (83-4, 1989, MRID No. 41348601, 42901401) to be acceptable and the data evaluation record (HED Doc. No. 010725) to be adequate. The systemic/reproductive toxicity NOEL and LOEL were 2 and 14 ppm (0.1 and 0.7 mg/kg/day) based on cytoplasmic vacuolation of epithelial ductal cells of epididymis. At 100 ppm (5 mg/kg/day), histopathological findings in the epididymis were accompanied by increased epididymal weight, reduced fertility, and decreased pup weight gain and viability. The NOEL and LOEL for plasma ChE and RBC and brain AChE were 2 and 14 ppm based on inhibition in adults and weanling pups.

The Committee considered the older 3-generation reproduction toxicity study in rats (83-4, 1969, MRID No. 00081115) to be unacceptable and the data evaluation record (HED Doc. No. 004239) to be inadequate based on current standards.

The Committee considered the developmental toxicity study in rats (83-3a, MRID No. 40329401) to be acceptable and the data evaluation record (HED Doc. No. 011768) to be adequate. The maternal toxicity NOEL and LOEL were 4.2 and 18 mg/kg/day, respectively, based on clinical signs of toxicity (including tremors, lacrimation, exophthalmos, hyperactivity, urine stains) and decreased body weight gain during dosing. The developmental toxicity NOEL and LOEL were 4.2 and 18 mg/kg/day, respectively, based on increased resorptions. The LOEL for plasma ChE and RBC and brain AChE inhibition was 1 mg/kg/day, the lowest dose tested, based on deceased activity in dams and decreased brain AChE in day 20 fetuses.

The Committee considered the developmental toxicity study in rabbits (83-3b, 1987, MRID No. 40464701) to be acceptable and the data evaluation record (HED Doc. No. 011768) to be adequate. The maternal toxicity NOEL and LOEL were 1 and 2.75 mg/kg/day based on soft stools. The developmental toxicity NOEL and LOEL were 2.75 and 7.5 mg/kg/day, based on increased resorptions, equivocal decreases in mean fetal weight and increases in unossified metacarpals. The NOEL and LOEL for plasma ChE and RBC and brain AChE were 1 and 2.75 mg/kg/day based on decreased activity in dams.

The Committee considered the older developmental toxicity study in rabbits (1982, 83-3b, MRID No. 00132347) to be acceptable and the data evaluation record (HED Doc. No. 004239) to be adequate. The maternal toxicity NOEL and LOEL were considered to be 6 and 18 mg/kg/day, respectively, based on clinical signs (dyspnea, diarrhea, clonic muscle spasms, salivation), decreased body weight gain and food consumption, increased death of dams (11/20), and increased abortions. The developmental toxicity NOEL and LOEL were considered to be 2 and 6 mg/kg/day based on increased resorptions.

The Committee recommended that a developmental neurotoxicity study be conducted based upon reductions in brain AChE observed in rat fetuses and neurotoxic effects observed in the adults.

D. Acute and Subchronic Neurotoxicity:

The Committee considered the acute delayed neurotoxicity study in hens (81-7, MRID No. 40229201) and the 90-day neurotoxicity study in hens (82-5, MRID No. 40933601) to be acceptable and the data evaluation records of these studies (HED Doc. No. 008227, 008289; 009632) to be adequate.

There were no acute or subchronic neurotoxicity studies in rats (81-8 and 82-7) available for review by the Committee. The Committee recommended that acute and subchronic neurotoxicity studies in rats be submitted to the Agency. The Committee was informed, however, that the studies are expected to be received by the Agency in 1997. A special non-guideline neurotoxicity study (Veronesi et al, 1990, no MRID No.:) from the literature was also noted and this study indicated possible neuropathology in the brain. This issue will be reinvestigated when the series 81-8 and 82-7 acute and subchronic neurotoxicity studies are reviewed.

E. Mutagenicity:

The Committee considered the following studies to be acceptable:

1) Salmonella assay (MRID No. 41077501, HED Doc. No. 009620): the test is negative up to 5000 μg/plate, the highest concentration tested.

2) Mouse micronucleus (MRID No. 41451701, HED Doc. No. 008387): the test is weakly positive at a dose level of 150 mg/kg (weak response: 4.5 micronuclei/1000 PCE vs. control 1.3/1000 PCE at 12 hour sampling interval).

3) Unscheduled DNA synthesis (UDS)/primary rat hepatocytes (MRID No. 41726301, HED Doc. No. 008413): the test is positive at a concentration of 5 μg/ml or higher.

The Committee considered the following studies to be unacceptable:

1) Mouse micronucleus (MRID No. 00132353, HED Doc. No. 004239): the test is negative, but the protocol is not acceptable.

2) E. coli pol test for DNA damage/repair (MRID No. 00147316, HED Doc. No. 004740): the test is negative, but no there was no evidence of toxicity (growth inhibition) and no evidence of compound diffusion from disc.

3) A mouse dominant lethal study on record (MRID No. 00132352, HED Doc. No. 004239), performed in 1970s, judged by the original reviewer as acceptable: the test is negative up to 25 mg/kg, the highest dose level tested. However, there are uncertainties about the study because of the very short review. The review indicated dosing may be adequate; presence of pre-implantation loss and absence of post-implantation loss.

There were also published studies indicating mixed responses, i.e. weak activity or no activity across several endpoints including Salmonella typhimurium reverse mutation test with and without metabolic activation, sister chromatid exchange (SCE) in

cultured cells in the presence or absence of metabolic activation and unscheduled DNA synthesis (UDS) in human fibroblasts.

Overall, the Committee concluded that the three acceptable studies satisfy the minimum initial battery for the three categories of mutagenicity testing as per the pre-1991 requirement. Based on the positive results in the in vivo micronucleus assay and the UDS assay, further testing for possible germ cell effects is necessary. The suggested test is the dominant lethal assay. Although a dominant lethal assay is available on this chemical, the test is very old, and it has uncertainties associated with it and a new one needs to be performed.

F. Reference Dose (RfD):

The Committee recommended that an RfD for this chemical be established based upon a comprehensive assessment of plasma ChE and RBC and/or brain AChE inhibition in humans, monkeys, rats, dogs and mice as a result of exposure to Fenthion. The findings of these studies are outlined above.

The data from all these studies indicate that: 1) interspecies variability and/or susceptibility of ChE or AChE to Fenthion is not a major factor; 2) plasma ChE is usually more susceptible than RBC or brain AChE to Fenthion inhibition but the differences are not always large and differed in the species tested; 3) differences in the susceptibility of males and females were also variable among the different species, females, however, were more susceptible in monkeys but females were not tested in humans.

For practical purposes, the Committee used the threshold NOEL/LOEL of 0.02 mg/kg/day for plasma ChE inhibition to set the RfD for this chemical. It should be noted that 0.02 mg/kg/day was also considered to be a threshold NOEL/LOEL in the human study. However, because of the human study shortcomings such as the limited number of subjects in conjunction with the lack of data on females, the Committee felt that the primate study would be more reliable for this purpose.

An uncertainty factor (UF) of 10 was applied to account for intra-species variability. The Committee felt that no uncertainty factor for inter-species extrapolation would be required since interspecies variability was not evident in this case. However, an additional UF of 3 was applied to account for the lack of a definite NOEL for the monkey and human studies, the lack of data on females in the human study, and the fact that brain AChE was inhibited at dose levels comparable to those causing plasma cholinesterase inhibition in some species. On this basis, the RfD was estimated to be 0.0007 mg/kg/day.

It should be emphasized here that this value also provides adequate protection against other systemic effects seen in the rat study such as effects on the epididymis and on the visual system where females were more susceptible than males. For example, the effects on the rat ocular system demonstrated a NOEL and LOEL of 0.3 and 1.3 mg/kg/day, respectively, in females and 0.8 and 5.2 mg/kg/day in males. In males, the effects on the epididymis had a NOEL and LOEL of 0.2 and 0.8 mg/kg/day. If the RfD was to be based on the NOEL for ocular effects in females using a UF of 100, the RfD would be 0.003 mg/kg/day, higher than that for using the threshold NOEL/LOEL for human and monkey plasma ChE data.

It should also be noted that this chemical has been reviewed by the FAO/WHO joint committee meeting on pesticide residue (JMPR) in 1972, 1976 and by FAO in 1978 and 1979 and that an estimate of acceptable daily intake (ADI) of 0.001 mg/kg/day for man has been established. In the JMPR evaluation, the following studies were considered to be significant: 1) a chronic toxicity study in rats with a NOEL of 0.15 mg/kg/day, a long-term toxicity study in dogs with a NOEL of 0.09 mg/kg/day, a toxicity study in monkeys with a NOEL of 0.07 mg/kg/day, and a toxicity study in human subjects with a NOEL of 0.02 mg/kg/day.

G. Individuals in Attendance:

Peer Review Committee members and associates present in the meeting of February 23, 1995 were William Burnam (Chief, SAB; Chairman, RfD/Peer Review Committee), George Ghali (Manager, RfD/Peer Review Committee), Karl Baetcke (Chief, TB I), Marcia Van Gemert (Chief TB II), Kerry Dearfield, Susan Makris, Melba Morrow, William Sette, Henry Spencer, James Rowe and Rick Whiting.

Peer Review Committee members and associates present in the meeting of October 5, 1995 were William Burnam (Chief, SAB; Chairman, RfD/QA Peer Review Committee), George Ghali (Manager, RfD/QA Peer Review Committee), Karl Baetcke (Acting Chief, TB II), Marion Copley (Acting Chief TB I), Guruva Reddy, William Sette, Henry Spencer and Rick Whiting. In attendance also was Kit Farwell, Hugh Pettigrew and Paula Deschamp of HED as observers.

Scientific reviewers (Committee or non-committee member(s) responsible for data presentation; signature(s) indicate technical accuracy of panel report)

John Doherty

Marion Copley

Respective Branch Chief (Committee member; signature indicates concurrence with the peer review unless otherwise stated)

Karl Baetcke

CC: Stephanie Irene
Debra Edwards
Marion Copley
Karl Baetcke
John Doherty
Albin Kocialski
Karen Whitby
Paula Deschamp
Beth Doyle
Amal Mahfouz (OW)
RfD File
Caswell File

H. Material Reviewed:

1. Christenson, W. R. (1990). Combined chronic toxicity/ oncogenicity study of technical grade Fenthion (Baytex) with rats. MRID No. 41743101, HED Doc. No. 009870. Classification: Core-minimum data. This study satisfies data requirement 83-5 or 83-1a and 83-2a of Subpart F of the Pesticide Assessment Guideline for chronic toxicity/carcinogenicity testing in rats.

2. Storrs, E. et al. (1979). Bioassay of Fenthion for possible carcinogenicity. MRID No. 00147478, 00132342, HED Doc. No. 004239. Classification: Core-supplementary data. This study does not satisfy data requirement 83-5 or 83-1a and 83-2a of Subpart F of the Pesticide Assessment Guideline for chronic toxicity/carcinogenicity testing in rats.

3. Leser, K. H. (1988). "E 1752" Oncogenicity study on B6C3F1 mice. MRID No. 41869201, 42759701, 42901403, HED Doc. No. 009536, 010324, 010725. Classification: Core-Guideline data. This study satisfies data requirement 83-2b of Subpart F of the Pesticide Assessment Guideline for carcinogenicity testing in mice.

4. Storrs, E. et al. (1979). Bioassay of Fenthion for possible carcinogenicity. MRID No. 00147478, 00132342, HED Doc. No. 004239. Classification: Core-supplementary data. This study does not satisfy data requirement 83-2b of Subpart F of the Pesticide Assessment Guideline for carcinogenicity testing in mice.

5. Christianson, W. R. (1990). Chronic feeding toxicity study of Fenthion technical (Baytex) with dogs. MRID No. 41632801, 42901402, HED Doc. No. 009295, 010725. Classification: Core-Guideline data. This study satisfies data requirement 83-1b of Subpart F of the Pesticide Assessment Guideline for chronic toxicity testing in dogs.

6. Hoffman, K. et al. (1975). Fenthion: Chronic toxicity study in dogs. MRID No. 00132341, HED Doc. No. 004239. Classification: Core-Supplementary data. This study does not satisfy data requirement 83-1b of Subpart F of the Pesticide Assessment Guideline for chronic toxicity testing in dogs.

7. Griffin, T. (1979). Safety evaluation of Fenthion in human volunteers. MRID No. 00147246, HED Doc. No. 011768. Classification: Core-Supplementary data. This study was not conducted to fulfill a specific data requirement of Subpart F of the Pesticide Assessment Guideline.

9. Rosenblum, L. (1980). A safety evaluation of Fenthion (S1752) in Rhesus monkeys (Macca mulatta). MRID No. 00147245, HED Doc. No. 011768. Classification: Core-Supplementary data. This study was not conducted to fulfill a specific data requirement of Subpart F of the Pesticide Assessment Guideline.

10. Kowalski, R. L. et al. (1989). A two-generation reproduction study with Fenthion (Baytex) in the rat. MRID No. 41348601, 42901401, HED Doc. No. 008545, 010725. Classification: Core-Guideline data. This study satisfies data requirement 83-4 of Subpart F of the Pesticide Assessment Guideline for reproductive toxicity testing in rats.

11. Loser, E. and Lorke, D. (1969). Bay 29493: Generation tests on rats. MRID No. 00081115, HED Doc. No. 004239. Classification: Core-Supplementary data. This study does not satisfy data requirement 83-4 of Subpart F of the Pesticide Assessment Guideline for reproductive toxicity testing in rats.

12. Kowalski, R. L. et al. (1987). A teratology study with Fenthion (Baytex technical) in the rat. MRID No. 40329401, HED Doc. No. 011768. Classification: Core-minimum data. This study satisfies data requirement 83-3a of Subpart F of the Pesticide Assessment Guideline for developmental toxicity testing in rats.

13. Clemens, G. R. et al. (1987). A teratology study in the rabbits with Fenthion (Baytex technical). MRID No. 40464701, HED Doc. No. 011768. Classification: Core-Guideline data. This study satisfies data requirement 83-3b of Subpart F of the Pesticide Assessment Guideline for developmental toxicity testing in rabbits.

14. Becker, H. et al. (1982). Embryotoxicity and teratogenicity study on S 1752 in rabbits. MRID No. 00132347, HED Doc. No. 004239. Classification: Core-minimum data. This study satisfies data requirement 83-3b of Subpart F of the Pesticide Assessment Guideline for developmental toxicity testing in rabbits.

15. Hays, R. H. and Ramm, W. W. (1988). Subchronic delayed neurotoxicity study of Fenthion technical (Baytex) with hens. MRID No. 40933601, HED Doc. No. 009632. Classification: Core-minimum data. This study satisfies data requirement 82-5 of Subpart F of the Pesticide Assessment Guideline for 90-day delayed neurotoxicity testing in hens.

16. Flucke, W. and Kaliner, G. (1987). E 1752 Acute neurotoxicity studies on hens following oral and dermal administration. MRID No. 40229201, HED Doc. No. 008227. Classification: Core-Guideline data. This study satisfies data requirement 81-7 of Subpart F of the Pesticide Assessment Guideline for neurotoxicity testing in hens.

17. Herbold, B. A. (1990). E-1752 Salmonella/microsome test. MRID No. 42077301, HED Doc. No. 009620. Classification: Acceptable. This study satisfies data requirement 84-2 of Subpart F of the Pesticide Assessment Guideline.

18. Lehn, H. (1990). E 1752 c. n. Fenthion mutagenicity test on unscheduled DNA synthesis in rat liver primary call cultures in vitro. MRID No. 41726301, HED Doc. No. 008413. Classification Acceptable. This study satisfies data requirement 84-2 of Subpart F of the Pesticide Assessment Guideline.

19. Herbold, B. A. (1990). E-1752 micronucleus test on the mouse. MRID No. 41451701, HED Doc. No. 008387. Classification: Acceptable. This study satisfies data requirement 84-2 of Subpart F of the Pesticide Assessment Guideline.

20. Machemer, L. and Lorke, D. (1978). S-1752 (Fenthion): Dominant lethal study on male mice to test for mutagenic effects. MRID No. 00132352, HED Doc. No. 004239. Classification: Acceptable. This study satisfies data requirement 84-2 of Subpart F of the Pesticide Assessment Guideline.

21. Herbold, B. and Lorke, D. (1978). S-1752 (Fenthion): Micronucleus test on mouse to evaluate S 1752 for mutagenic potential. MRID No. 00132353, HED Doc. No. 004239. Classification: Unacceptable. This study does not satisfy data requirement 84-2 of Subpart F of the Pesticide Assessment Guideline.

22. Herbold, B. (1983). E-1752 Pol test on E. coli to evaluate for potential DNA damage. MRID No. 00147316, HED Doc. No. 004740. Classification: Unacceptable. This study does not satisfy data requirement 84-2 of Subpart F of the Pesticide Assessment Guideline.

23. Veronesi, B., Jones, K. and Pope, C. (1990). The Neurotoxicity of Subchronic Acetylcholinesterase (AChE) Inhibition in the Rat. Toxicology and Applied Pharmacology 104: 440-456.