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MEMORANDUM

ABATE

SUBJECT: *TEMEPHOS* - Report of the Hazard Identification Assessment Review Committee.

FROM: David S. Liem, Ph.D
Reregistration Branch II
Health Effects Division (7509C)
and
Jess Rowland, Executive Secretary
Hazard Identification Assessment Review Committee
Health Effects Division (7509C)

THROUGH: K. Clark Swentzel, Chairman,
Hazard Identification Assessment Review Committee
Health Effects Division (7509C)
and
Mike Metzger, Co-Chairman
Hazard Identification Assessment Review Committee
Health Effects Division (7509C)

TO: Nicole Paquette, Risk Assessor
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PC Code: 059001

On April 7, 1998 the Health Effects Division's Hazard Identification Assessment Review Committee evaluated the toxicology data base of *Temephos*, selected the toxicological endpoints for acute and chronic dietary as well as short, intermediate and long-term occupational/residential exposure risk assessments, evaluated the carcinogenic potential, and addressed the potential sensitivity of infants and children as required by the Food Quality Protection Act (FQPA) of 1996. The Committee's conclusions are presented in this report.

1/15

Committee Members in Attendance

Members present were: Karl Baetcke, William Burnam, Karen Hamernik, Susan Makris, Mike Metzger, Melba Morrow, Jess Rowland (Executive Secretary) and Clark Swentzel (Chairperson). Member in absentia: Robert Fricke. Data was presented by David Liem of Reregistration Branch II.

Also in attendance were Jonathan Becker, Joycelyn Stewart, Pauline Wagner, Nicole Paquette, Larry Schnaubelt, Jim Goodyear, Bill Evans and Ron Parker.

Data Presentation:
and
Report Presentation

David S. Liem
Toxicologist

Report Concurrence:

Jess Rowland
Executive Secretary

I. INTRODUCTION

The Agency issued a Registration Standard for Temephos [O,O'-(thiodi-4,1-phenylene)bis(O,O-dimethylphosphorothioate)] in August 1981. The tolerance of 0.1 ppm established for combined negligible residues for Temephos and its sulfoxide in/on orange and tangerine groves in Arizona and California has been withdrawn by the Registrant. At the present time Temephos is primarily used as a mosquito larvacide, applied in granular or liquid forms, in restricted areas on an-as-needed basis. The use sites include outdoor non-food and non-domestic aquatic areas such as standing waters, ponds, lakes, tidal waters, catch basin, marshlands, margins of streams, and intertidal zones of sandy beaches with Florida, New Jersey and California being the primary user States.

On April 7, 1998 the Health Effects Division's Hazard Identification Assessment Review Committee (HIARC) evaluated the toxicology data base to select the toxicological endpoints for acute and chronic dietary as well as short, intermediate and long-term occupational/residential exposure risk assessments. In addition the HIARC, evaluated the carcinogenic potential and addressed the potential sensitivity of infants and children as required by the Food Quality Protection Act (FQPA) of 1996.

II. HAZARD IDENTIFICATION

A. Acute Reference Dose (RfD)

Study Selected: None

MRID No.: None

Executive Summary: None

Dose and Endpoint for Risk Assessment: Not Applicable

Comments about Study/Endpoint: Since there are no registered food-uses at the present time, an acute dietary risk assessment is not required.

Uncertainty Factor (UF): None

This risk assessment is **Not** required

B. Chronic RfD

Study Selected: None

MRID No.: None

Executive Summary: None

Dose and Endpoint for Risk Assessment: Not Applicable

Comments about Study/Endpoint: Since there are no registered food-uses at the present time, a chronic dietary risk assessment is not required. Thus, a Reference Dose was not established.

Uncertainty Factor (UF): None

This risk assessment is **Not** required

C. Occupational/Residential Exposure

There are no registered residential uses at the present time. Therefore, the following risk assessments are applicable only for occupational exposure.

1. Dermal Absorption

Dermal Absorption Factor: No dermal absorption studies are available. The Committee assumed a dermal factor of 100% (default value). This assumption is supported by similar toxicity effects at comparable dose levels in developmental oral and dermal studies in rabbits (MRID#00101659 and 00101660).

2. Short-Term Dermal - (1-7 days)

Study Selected: 90-Day Feeding Study in Rats

§82-1a

MRID No.: 00001239

Executive Summary: In a subchronic toxicity study, groups of rats (45 rats/dose/sex) were fed Temephos (purity 96.4%) in their diet at levels of 2, 6, or 18 ppm (equivalent to 0.1, 0.3 or 0.9 mg/kg/day) for 92 days to determine the highest dietary level which would not inhibit plasma, RBC or brain cholinesterase activity.

Another group of 45 rats/sex/group was fed with a diet containing Temephos at 350 ppm (17.5 mg/kg/day) dose level to determine a maximum tolerated dose and to induce histopathological effects. There were 65 rats/sex in the control

group. Seven controls of each sex and 4 rats/sex/dose group were sacrificed at 1, 3, 5, 9 and 13 weeks of the study period for RBC, plasma and brain cholinesterase activity evaluation. ChE activity was also evaluated on four rats of each sex at week 12 of the study dosed at 350 ppm. At week 13 all survivors were given control diet and recovery of the ChE activity was determined 2 and 4 weeks later. One control male and one female each of the 6 and 18 ppm dose groups died during the study. At 350 ppm the female body weight gain was significantly depressed as compared to the controls. No treatment related changes were observed in clinical sign observations, ophthalmology evaluations and food consumption, clinical chemistry and hematology evaluations at all dose levels. No gross and microscopic treatment-related changes were noted in any dose group during the study. The liver/body weight ratio of the 2 and 350 ppm males and the 18 ppm females were significantly decreased as compared to the controls. Since dose-related trends in the liver/body weight ratio were not evident, these decreases are not considered to be treatment-related. Because the greatest decrease in the liver/body weight ratio occurred in the 350 ppm males (-23% of control), this is judged to be treatment-related. Decreased RBC cholinesterase activity was noted in the 6 ppm males at weeks 9 and 13 (75% and 84% of control, respectively) and in 18 ppm males and females throughout the treatment period (64-85% and 65-89% of control, respectively). Significantly decreased RBC cholinesterase activity was noted in the 350 ppm males and females (8% and 11% of control, respectively) at week 12 (only measured time period). The RBC ChE activity decrease in the 18 and 350 ppm males and females were judged to be dose-related. RBC ChE activity decrease in the 6 ppm males (84% and 83% of controls, on weeks 9 and 13, respectively) was considered to be a borderline occurrence. Only the plasma cholinesterase activity was significantly depressed at 350 ppm in males and females at week 13 (52% and 39% of control, respectively) and this is judged to be treatment-related. Significant decrease in the brain cholinesterase activities was noted in males and females dosed at 350 ppm at week 13 (23% and 22% of females, respectively). Inhibition of the brain ChE activity in the 18 ppm males and females in the first five weeks of the study was also noted (81-85% and 81-91% of controls, respectively); these effects disappeared after the five weeks. Therefore this inhibition was considered borderline occurrence.

Since RBC ChE activity inhibition at 6 ppm and brain ChE activity inhibition at the 18 ppm were considered to be equivocal, the registrant repeated this current study at dietary levels of 0, 6, 18 and 54 ppm to ascertain if borderline ChE activity inhibitions seen in this study were a definite and reproducible effect. In the repeat study (MRID No. 00001356), statistically significant decreases in RBC cholinesterase activity was seen in both sexes at 18 and 54 ppm.

The systemic LOEL is 350 ppm (17.5 mg/kg/day) based on decreased body weight (15%) and liver/body weight ratio (23%). The systemic NOEL is 18 ppm (0.9 mg/kg/day). The ChE LOEL for this subchronic study is 18 ppm (0.9

mg/kg/day), based on inhibition of RBC cholinesterase activity in both sexes. The ChE NOEL is 6 ppm (0.3 mg/kg/day).

Dose and Endpoint for Risk Assessment: NOEL=0.3 mg/kg/day based on inhibition of RBC cholinesterase activity observed in both sexes at 0.9 mg/kg/day (LOEL) as early as one week.

Comments about Study/Endpoint: The toxic effect [(RBC cholinesterase inhibition (ChEI)] was observed within one week after initiation of treatment which is appropriate for this exposure period of concern (i.e., 1-7 days).

Since an oral NOEL was selected, a dermal absorption factor of 100% should be used for this dermal risk assessment.

In addition, the dose and endpoint of this study is supported by the similar dose (NOEL=0.3 mg/kg/day) and endpoint (RBC ChEI) seen in another subchronic toxicity study in rats (MRID#00001356) as well as a chronic study in dogs (MRID# 00001240) with a NOEL of 0.46 mg/kg/day based on RBC, plasma, and brain ChEI at 12.5 mg/kg/day (LOEL) where RBC and plasma ChE I occurred from week 1 onward.

Although, two 21-day dermal toxicity studies are available, the HIARC decided to use the 90-day oral toxicity study since the dermal studies were inadequate for use in risk assessments. In the study with rats where a formulation product was tested, there was no evaluation of cholinesterase activity (MRID# 00001238). In the other 21-day dermal study with rabbits where the technical product was tested, there were inadequate numbers of test animals for measurement of cholinesterase parameters (MRID#00101664).

This risk assessment is required.

3. Intermediate-Term Dermal (7 Days to Several Months)

Study Selected: 90-day Subchronic Feeding study in Rats

§82-1

MRID No.: 00001239

Executive Summary: See Short-Term Dermal.

Dose and Endpoint for Risk Assessment: NOEL=0.3 mg/kg/day based on inhibition of RBC cholinesterase activity observed at 0.9 mg/kg/day (LOEL) in both sexes.

Comments about Study/Endpoint: See Short-Term Dermal. Since an oral NOEL was selected, a dermal absorption factor of 100% should be used for this dermal

risk assessment.

This risk assessment is required.

4. Long-Term Dermal (Several Months to Life-Time)

Study Selected: 90-Day Feeding Study in Rats

§82-1a

MRID No.: 00001239

Executive Summary: See Short-Term Dermal .

Dose and Endpoint for Risk Assessment: NOEL=0.3 mg/kg/day based on inhibition of RBC cholinesterase activity observed at 0.9 mg/kg/day (LOEL) in both sexes.

Comments about Study/Endpoint: See Short-Term Dermal. Since an oral NOEL was selected, a dermal absorption factor of 100% should be used for this dermal risk assessment.

This risk assessment is required.

5. Inhalation Exposure (Any Time period).

Based on the LC₅₀ values of 0.2 mg/l technical Temephos is placed in Toxicity Category III/IV. The HIARC determined that there is no hazard by the inhalation route due to the lack of toxic effects near or above the limit dose. However, the current use pattern (5 days/week for 6 warm months and 2-3 times/week for the rest of the year), indicate a concern for potential inhalation exposure for pesticide handlers (applicators/mixers/loaders). **Therefore, the HIARC recommended the oral NOEL of 0.3 mg/kg/day for inhalation exposure risk assessments for any time period.** The following steps must be used for these risk assessments:

Step I. The inhalation exposure component (i.e. µg a.i./day) using 100% absorption rate (default value) and application rate should be converted to an **equivalent oral dose** (mg/kg/day).

Step II. The dermal exposure component (mg/kg/day) using a 100% dermal absorption rate and application rate should be converted to an **equivalent oral dose**. This dose should then be combined with the oral dose in Step I.

Step III. The combined dose from Step II should then be compared to the oral NOEL of 0.3 mg/kg/day to calculate the MOE's.

This risk assessment is required.

D. Margins of Exposure for Occupational/Residential Exposures

There are no registered residential uses for Temephos at the present time. A Margins of Exposure of 100 is adequate for occupational exposure risk assessments.

E. Recommendation for Aggregate Exposure Risk Assessments

Aggregate exposure risk assessments are not required since Temephos is not registered for food or residential uses at the present time and according to EFED exposure via drinking water is unlikely.

III. CLASSIFICATION OF CARCINOGENIC POTENTIAL

1. Combined Chronic Toxicity/Carcinogenicity Study in Rats

MRID No.: 000001385 and 000001386

Executive Summary: Groups of 60 rats/sex/group were fed a diets containing Temephos (purity 93.5%) at 0, 10, 100, and 300 ppm (\approx 0.5, 5.0, and 15 mg/kg/day) for two years. Rats used for the treated groups were derived from the offspring of 140 pregnant CD Sprague-Dawley rats that were treated with 100 ppm Temephos in the diet. The controls were from a separate shipment of the same strain of rats and age, derived from untreated female rats. No treatment-related effects were observed in survival, clinical signs, body weight/body weight gain, food consumption as well as in hematology, clinical chemistry and urinalysis parameters evaluated at 6 weeks, 3 months, 12 months and at termination of the study. There was a slight increase in absolute liver weight and liver/body weight ratio of both sexes of rats at 300 ppm (absolute weight: 8% in σ and 14% in ♀ , and relative liver weight, 18% in σ and 6% in ♀). However, since dose-related trends were not evident in either sex, these increases were not judged to be related to treatment. The most frequently noted gross pathology finding was mammary masses.

Histopathologically, these masses were identified as adenocarcinomas. These tumor incidences are evenly distributed among all groups (18, 21, 19 and 18 in the control, 10, 100, and 300 ppm females, respectively). Pituitary adenomas were also frequently noted in all groups, and no differences were noted as compared to their respective controls. Since no treatment-related trends were evident, these mammary adenocarcinoma and pituitary adenoma findings were not considered to be treatment-related. For chronic toxicity, the NOEL was \geq 300 ppm; a LOEL was not established.

Discussion of Tumor Data: There is no evidence of carcinogenicity.

Adequacy of the Dose Levels Tested: The Committee considered that the doses tested were adequate to test the carcinogenic potential of the test compound.

2. Carcinogenicity Study in Mice

The HIARC noted that a carcinogenicity study in a second species (mice) was not available and is not required for a non-food use chemical.

IV. FOPA CONSIDERATIONS

1. Neurotoxicity:

No evidence of organophosphate induced delayed neurotoxicity or neuropathology was observed in three acute delayed neurotoxicity studies in hens; however, these studies were judged to be inadequate for various technical deficiencies (MRID Nos. 00001364; 0010657 and 00161117).

There are data gaps for acute or subchronic neurotoxicity studies in rats.

2. Developmental Toxicity

In a prenatal **oral** developmental toxicity study, pregnant New Zealand rabbits received oral administration of Temephos (90.4%) in Tween 80 (1%) and deionized water at 0, 3, 10, or 30 mg/kg/day during days 6 through 18 of gestation.. No maternal or developmental toxicity was seen at the highest dose tested (30 mg/kg/day). This study was classified as unacceptable since the highest dose tested was inadequate to elicit maternal toxicity and thus evaluate the developmental toxicity potential of Temephos (MRID No. 00101660).

In a prenatal **dermal** developmental toxicity study, pregnant New Zealand rabbits received repeated dermal applications of Abate formulations at 0, 12.5, 25 or 50 mg/kg/day during days 6 through 18 of gestation. For maternal toxicity, the NOEL was 25 mg/kg/day and the LOEL was 50 mg/kg/day based on decrease in body weights. For maternal cholinesterase inhibition, the LOEL was 12.5 mg/kg/day based on plasma cholinesterase inhibition (brain ChE activity was not evaluated); a NOEL was not established. For developmental toxicity, the NOEL was ≥ 60 mg/kg/day (HDT); LOEL was not attained. It was noted that the test material in this study was the formulation products and not the technical material (MRID No. 00101659)..

3. Reproductive Toxicity:

One-generation and a three-generation reproduction studies were conducted with Temephos. The original study report for this one generation study was not available to confirm the reported symptoms of organophosphate induced poisoning in adult rats. The three generation study is classified as unacceptable for regulatory purposes.

In a one-generation reproduction study (MRID#: 00001368), a group of male and female rats (# unknown) was fed in the diet at 500 ppm (approximately 25 mg/kg/day) Temephos (90%) at the time they were placed together for breeding. Dosing was maintained through mating, gestation, parturition and lactation. Based on the results of the study, no significant differences in the fertility (pregnancy/matings), gestation (litters born alive/pregnancies), viability (pups surviving/pups born alive) and lactation indices for the Temephos-fed animals were observed compared with the controls. Numbers of litters and pups born alive and mean pup weight at weaning were comparable among the dose groups; number of litters (15 from 15 matings) were produced and litter size averaged 10.5. Some 500 ppm Temephos-treated rats (# not indicated) showed signs of ChE poisoning. Based on the data as presented in the study report, administration of Temephos at 500 ppm (25 mg/kg/day) in the diet, had no adverse effects on the reproduction and lactation performance of rats. The toxicity endpoint was not verified because the original report was not found. The reproductive NOEL is > 500 ppm (25 mg/kg/day) (HDT). The systemic ChE NOEL is < 500 ppm (25 mg/kg/day).

This study **may be classified as acceptable** for a one-generation reproduction study in rats (83-4), pending further review of the original study report. The original study review was not found.

In a 3-generation reproduction toxicity study (MRID#: 00001366 and 00001388), Temephos (87.1% a.i.) was fed in the diet to rats at dose levels of 0, 25, and 125 ppm (0, 1.25, and 6.25 mg/kg/day). For the P generation, 24 rats/dose were mated once. For the F₁ generation, 16 rats/dose were mated once, and for the F₂ generations, 16 rats/dose were mated twice. In each generation, rats were mated when they were 3-4 months old. The pups were weaned directly onto the respective dose levels of their parents. The size of the litters were reduced to 10 pups on the fifth day after birth. This study was conducted as per standard procedures for a 3-generation reproduction study. Body weights of adult rats were comparable among the dose groups in all generations; slight decreases (<10%) in body weights were noted in the 125 ppm F₁ and F₂ males and females, but since the difference was small and dose-related trends were not evident, these decreases were not judged to be treatment-related. The gestation, viability and lactation indices for the P generation were comparable among the groups; slight decreases of the 25 and 125 ppm fertility indices and the 125 ppm pup weights as compared to the controls were noted, but they are not judged to be treatment-related. The fertility, gestation, viability and lactation indices for the F₁ generation were comparable among the groups; a slight decrease in the 25 and 125 ppm pup weights as compared to the controls is not judged to be treatment-related. No adults died during the reproduction and lactation periods.

The fertility, gestation and lactation indices for the **first mating** of the F₂ generation were comparable among the groups. Since a decrease in the 125 ppm pup viability index was noted as compared to the controls (82% versus 94%), a second mating was conducted for the F₂ rats. No F₂ adults died during the reproduction and lactation periods in the first mating. In the **second mating** of the F₂ generation, one 25 ppm female died after delivering 6 dead pups. Two controls and four 25 ppm females failed to conceive. The fertility, viability, and lactation indices of the 125 ppm dose group exceeded the controls. Since the viability index of the 125 ppm dose group was higher than the controls (99% versus 83%), the low viability index of 82% noted in the F₂ first mating is judged to be coincidental and hence not related to treatment. Overall the differences noted in the reproduction data in the F₂ are not judged to be related to treatment. Gross observations without necropsy were conducted on all P and F₁ pups. Gross and microscopic evaluations were conducted for all F₂ pups of the control and 125 ppm groups. No consistent gross and microscopic effects were noted. However, a number of spleen hematopoiesis in pups were noted (20% in the control and 17% in the 125 ppm dose group); spleen hematopoiesis is a common occurrence in pups up to weaning.

Based on the results of the study, the fertility (pregnancy/matings), gestation (litters born alive/pregnancies), viability (pups surviving 5 days/pups born alive) and lactation (pup weaned/remaining pups after litter reduced at 5 days) indices for the Temephos-fed animals were comparable with the controls. The combined (of all matings) mean pup weight at weaning was slightly higher in the 25 ppm dose group and slightly lower in the 125 ppm dose group as compared to the controls. There was a slight reduction in mean pup weights at weaning for both males and females in the 25 and 125 ppm P and in the 125 ppm F₁ generations. Based on the data as presented in the study report, administration of Temephos at 25 and 125 ppm in the diet, had no systemic toxicity and adverse effects on the reproduction and lactation performance of the rats were not noted.

For parental systemic toxicity, the NOEL was > 125 ppm (6.25 mg/kg/day, highest dose tested.). For offspring toxicity, the NOEL was also > 125 ppm (6.25 mg/kg/day, HDT).

This study is classified as **unacceptable-guideline** for a three-generation reproduction study in rats (§83-4) because only two instead of three treated groups were used. The lack of any signs of parental toxicity in the study even at 125 ppm (6.25 mg/kg/day) dose level suggests that this level was too low. Also, pups of the P and F₁ generations were not subjected to gross necropsy.

Based on the results of these studies, the HIARC concluded that an adequate evaluation of the reproductive toxicity of Temephos can not be made at the present time.

4. Additional information from the literature (IF AVAILABLE)

No additional information from the open literature are available.

5. Determination of Susceptibility

The HIARC determined that a determination of the increased susceptibility can not be made at this time since the studies required to make this determination are not available. (i.e., acute delayed neurotoxicity study in hen; acute and subchronic neurotoxicity studies in rats; prenatal developmental toxicity studies in rats and/or rabbits; and a two-generation reproduction study in rats).

6. Recommendation for a Developmental Neurotoxicity Study

The HIARC could not make a determination on the requirement of a developmental neurotoxicity study, due to the inadequate data base.

7. Determination of the FQPA Safety Factor:

A FQPA Safety Factor for the protection of infants and children from exposure to Temephos as required by FQPA will not be necessary since there are no registered food or residential uses and thus there are no concerns for potential exposures of Infants and Children to Temephos.

V. HAZARD CHARACTERIZATION

The toxicology database for temephos is inadequate with several data gaps and most of the available studies were conducted in the 60s and 70s and they do not meet the requirements of Subdivision F Guidelines. However, the available data are adequate to support the non-food use/non-residential use pattern.

In acute toxicity studies, temephos exhibits low-moderate toxicity depending on the route of exposure and the species used. Temephos has moderate acute toxicity (toxicity category II) by the oral route in rats and dermal route in rabbits, and is of low toxicity through an inhalation route in rats (Tox.Cat III). Temephos has a very low toxicity to the eyes in rabbits (Tox.Cat. III) and it is practically not a dermal irritant (Tox.Cat IV) and is not a dermal sensitizer.

In subchronic toxicity studies, the primary toxicological effect was neurotoxicity characterized by neurologic clinical signs and cholinesterase inhibition (ChEI) seen following multiple routes (gavage, dietary, and dermal) and multiple species (rats, rabbits and dogs). In rats, gavage doses as low as 0.45 mg/kg/day resulted in plasma and RBC ChEI. In a 21-day dermal toxicity study in rabbits, plasma and RBC ChEI were seen at 25 and 50 mg/kg/day, respectively.

A complete assessment of the neurotoxic potential of temephos could not be made since the available delayed neurotoxicity studies in hens are classified as unacceptable. Acute or subchronic neurotoxicity studies in rats are not available.

The database is inadequate to assess the developmental and reproductive toxicity of temephos. In a prenatal **oral** developmental toxicity study in pregnant rats, no maternal or developmental toxicity was demonstrated at the highest dose tested (30 mg/kg/day). This study was classified as unacceptable since the highest dose did not elicit any maternal toxicity, and thus the developmental toxicity potential of Temephos was not adequately evaluated.

In a prenatal **dermal** developmental toxicity study, repeated dermal application of a formulation product to pregnant rabbits resulted in maternal body weight decrease at 50 mg/kg/day and inhibition of plasma ChE activity at 12.5 mg/kg/day. Since a formulation was used in this study, this study is not acceptable for regulatory purposes.

In a three-generation reproduction study, no parental systemic or offspring toxicity was seen at the highest dose tested (125 ppm or 6.25 mg/kg/day). This study, was classified as unacceptable since only two doses were tested instead of three doses as required by the Subdivision F guidelines.

There are no data available from structurally-related chemicals which may be use to address the susceptibility issue. There was no evident of carcinogenicity.

No other information is available in the open literature which will indicate any other possible adverse effects.

VI. DATA GAPS

Acute Delayed Toxicity - Hen	§81-7
Acute Neurotoxicity -Rat	§81-8
Subchronic Neurotoxicity-Rat	§82-5
Developmental Toxicity -Rat or Rabbit	§83-3 a,b

VII. ACUTE TOXICITY

Acute Toxicity of Temephos

Guideline#	Study Type	MRID	Results	Tox Category
81-1	Acute Oral	00001902	LD ₅₀ = 444 mg/kg	II
81-2	Acute Dermal	140124 1906/1907	LD ₅₀ = 1850 mg/kg (Males) LD ₅₀ = 970 mg/kg (Females)	II II
81-3	Acute Inhalation	00101656	LC ₅₀ > 1.3 mg/L	III
81-4	Primary Eye Irritation	001907	Corneal opacity 72 hrs	III
81-5	Primary Skin Irritation	140124	PIS = 1.4	IV
81-6	Dermal Sensitization	00157836	Not a sensitizer	

VIII SUMMARY OF TOXICOLOGY ENDPOINT SELECTION

The doses and toxicological endpoints selected for various exposure scenarios are summarized below.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY	MOE
Acute Dietary	None	No registered food or residential uses; risk assessment is not required.		NA
Chronic Dietary	None	No registered food or residential uses; risk assessment is not required.		NA
Short-Term (Dermal) ^a	Oral NOEL = 0.3	RBC ChE Inhibition	90-day Feeding in Rats	100
Intermediate-Term (Dermal) ^a	Oral NOEL = 0.3	RBC ChE Inhibition	90-day Feeding in Rats	100
Long-Term (Dermal)	Oral NOEL = 0.3	RBC ChE Inhibition	90-day Feeding in Rats	100
Inhalation (Any Time Period) ^a	Oral NOEL = 0.3	RBC ChE Inhibition	90-day Feeding in Rats	100

^a = Since an Oral NOEL was selected a dermal absorption (100%) and inhalation absorption (100%) factors should be used for these risk assessments (i.e., corrected for dermal and inhalation exposures).