Appendix L. The HED Chapter of the Reregistration Eligibility Decision Document (RED) for Thiobencarb (Case Number 2665; Chemical number 108401)

MEMORANDUM

SUBJECT: The HED Chapter of the Reregistration Eligibility Decision Document (RED) for Thiobencarb (Case number 2665; Chemical number 108401)

FROM: Paul Lewis, Biologist
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THRU: Pauline Wagner, Chief
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and
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TO: Walt Waldrop, Acting Chief
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Please find attached the Human Health Risk Assessment for the Thiobencarb Reregistration Eligibility Decision Document (RED). This chapter includes the Hazard Assessment from Stephen Dapson in TBII (Attachment I), the Occupational and Residential Exposure Assessment from Tom Campbell in OREB (Attachment II), Product and Residue Chemistry Assessment from David Miller in CBRS (Attachment III), and the Dietary Risk Analysis from Brian Steinwand in SAB (Attachment IV). If you have any questions concerning this document, please call Paul Lewis at 305-7398.

Attachments

pc (without attachments): T. Campbell, OREB
S. Dapson, TBII
P. Deschamp, RCAB
D. Miller, CBRS
B. Steinwand, SAB

1. EXECUTIVE SUMMARY

Thiobencarb [S-((4-chlorophenyl)methyl)diethylcarbamothioate] is a thiocarbamate herbicide that is applied to rice, lettuce, celery and endives to control grasses and broadleaf weeds. It is applied as a liquid and granular using fixed-wing aircraft, helicopter, granular tractor-drawn spreader, and groundboom sprayer.

Thiobencarb is sold in the United States by Valent Corporation. There are five registered products: technical thiobencarb (EPA Reg. No. 63588-4; 97.4% a.i.), Valent Bolero 8 EC (EPA Reg. No. 59639-79), Valent Bolero 10 G (EPA Reg. No. 59639-80), Bolero 10 G (EPA Reg. No. 63588-5) and Bolero 8 EC (63588-6). Since thiobencarb is applied to food crops, EPA expects both dietary and occupational exposure (residential exposure is not expected since there are no residential uses).

II. SCIENCE ASSESSMENT

A. Physical Chemistry Assessment

Thiobencarb [S-((4-chlorophenyl)methyl)diethylcarbamothioate] is a thiocarbamate pesticide.

1. Identification of Active Ingredient

Thiobencarb is a pale, yellow liquid with a boiling point of 126-129 C. Thiobencarb is readily soluble in most organic solvents and slightly soluble in water. Its empirical formula is $C_{12}H_{16}ClNOS$ and its molecular weight is 257.8.

2. Manufacturing-Use Products

A search of the Reference Files System (REFS) conducted on 10/18/95 identified a single thiobencarb technical product (T) registered to K-I Chemical U.S.A., Incorporated under Shaughnessy No. 108401; the 97.4% T (EPA Reg. No. 63588-4). The K-I Chemical 97.4% T was transferred from Chevron Chemical Co. (12/5/91). Only the K-I Chemical TGAI and 97.4% T are subject to a reregistration eligibility decision.

3. Regulatory Background

The Thiobencarb Phase IV Review (dated 4/15/91 by C. Olinger and S. Funk) determined that Chevron data submissions for all product chemistry data requirements met the acceptance criteria for Phase V review. The Chevron data are applicable to the K-I Chemical 97.4% T, provided that K-I Chemical confirms that the manufacturing process and site have not changed since the product transfer. Otherwise, all product chemistry data will be required for the K-I Chemical 97.4% T.

The current status of the product chemistry data requirements for K-I Chemical thiobencarb TGAI and 97.4% T is presented in Appendix 1. Refer to this table for a listing of the outstanding product chemistry data requirements.

4. Conclusions

All pertinent data requirements are satisfied for the thiobencarb TGAI 97.4% pending confirmation by K-I Chemical that the manufacturing process and location have not changed since the product was transferred from Chevron. Provided that the registrant certifies that the suppliers of beginning materials and the manufacturing process for the thiobencarb technical product have not changed or submits a complete updated product chemistry data package, HED has no objections to the reregistration of thiobencarb with respect to product chemistry data requirements.

B. Human Health Assessment

1. Hazard and Dose Response Assessment

At present, the available toxicological database for thiobencarb is adequate and will support reregistration eligibility for the currently registered uses.

a. Acute Toxicity

Thiobencarb has been tested for acute toxicity by the oral, dermal and inhalation routes of exposure. The results obtained in these studies, which are listed in Table 1, satisfy the acute toxicity data requirements.

Table 1. Acute Toxicity Values for Technical Thiobencarb

TEST	RESULTS	TOXICITY CATEGORY	PURITY
Oral LD_{50} - rat	Males: LD_{50} = 1033 (924-1155) mg/kg Females: LD_{50} = 1130 (1033-1247) mg/kg (MRID 42130701)	III	96.0%
Dermal LD_{50} - rabbit	LD_{50} > 2000 mg/kg (both sexes) (MRID 42130701)	III	96.0%
Inhalation LC_{50} - rat	LC_{50} > 42.8 mg/L (1 hour) (MRID 00040585, 00134976	IV	95.1%
Eye Irritation - rabbit	Slight irritation (MRID 00040581)	III	95.1%

TEST	RESULTS	TOXICITY CATEGORY	PURITY
Dermal Irritation - rabbit	Slight irritation (MRID 00040583, 00081900)	IV	95.1%
Dermal Sensitization - guinea pig	Not a sensitizer (MRID 00161699)	NA	84.0%

b. Subchronic Toxicity

In a 21 day dermal study (MRID# 42893001, revision of MRID# 42003401), Sprague-Dawley rats received repeated dermal applications of Bolero® 8EC (85.2% a.i.) at doses of 0, 40, 160, or 500 mg/kg, 5 days per week, over a 22-day period. 36 animals of each sex were used, 6 animals/sex/dose for the 0, 40, 160 and 500 mg/kg dose plus an extra 6/sex/dose for the 0 and 500 mg/kg doses at recovery. There was a dose related increase in the incidence of skin irritation in treated versus control rats of both sexes. Six additional animals dosed with 0 and 500 mg/kg were held for 2 weeks following dosing as a recovery group. Reduced food intake with an associated reduction in body weight gain was observed in the mid- and high-dose groups. The reduction in body weight gain persisted in high-dose males in the recovery group. Statistically significant decreases in food efficiency were observed in mid-and high-dose males. For dermal toxicity, a NOEL was not observed and the LOEL was less than 40 mg/kg/day based on the skin irritation observed. For systemic toxicity, the NOEL was 40 mg/kg/day and the LOEL was 160 mg/kg/day based on decreases in body weight gain and food consumption in males and females, and statistically significant decreases in food efficiency in males.

Subchronic toxicity studies were conducted by Industrial Biotest (IBT) Laboratories and are classified as supplementary data, not adequate to satisfy Subdivision F guidelines. Therefore, the data requirements for subchronic studies in rats and dogs are satisfied by the chronic feeding studies in the rat and dog (see chronic toxicity and carcinogenicity section).

c. Chronic Toxicity

In a combined chronic toxicity/carcinogenicity feeding study (MRID# 00154506), Fischer 344 rats received 0, 20, 100 or 500 ppm (approximately 0, 1, 5, and 25 mg/kg/day by standard conversion methods) technical Bolero® (95.3% a.i.) in the diet for 2 years. Systemic toxicity was noted at 100 ppm and above as decreased body weight gain, food consumption and food efficiency. There was also an increase in blood urea nitrogen. However, no evidence of carcinogenicity at the dose levels tested was observed. For chronic toxicity, the NOEL was 1 mg/kg/day and the LOEL was 5 mg/kg/day based on decreased body weight gains, food consumption, food efficiency

and increased blood urea nitrogen.

In a chronic oral toxicity study (MRID# 00144742), Beagle dogs received 0, 1, 8, or 64 mg/kg/day of thiobencarb technical (Lot# SX-1381; Purity 96.3% a.i.) by capsule for 52 weeks. Systemic toxicity was noted in the high dose males as decreased body weight gains and increased absolute and relative kidney and liver weights in high dose males and females. There were decreases in serum albumin and protein in high dose males and females (a slight effect was noted in mid dose males). In addition, there were decreased erythrocyte counts and hemoglobin levels with a reduction in hematocrit in high dose males and females along with decreases in alanine aminotransferase and cholesterol levels in the high dose group. For systemic toxicity, the NOEL was 8 mg/kg/day and the LOEL was 64 mg/kg/day based on increased liver and kidney weights and decreased hematological and clinical chemistry parameters. Based on biologically significant depression in cholinesterase activity, for plasma cholinesterase, the NOEL was 1 mg/kg/day and the LOEL was 8 mg/kg/day; for erythrocyte cholinesterase, the NOEL was 8 mg/kg/day and the LOEL was 64 mg/kg/day; for brain cholinesterase the NOEL was equal to or greater than 64 mg/kg/day and the LOEL was greater than 64 mg/kg/day.

d. Carcinogenicity

In a carcinogenicity study (MRID# 00086004), B6C3F1 mice received 0, 25, 100, 400, or 1600 ppm (0, 3, 14, 56, and 235 mg/kg/day for males and 0, 5, 19, 75, and 302 mg/kg/day for females, respectively) technical Bolero® (93.7% a.i.) for 104 weeks. Systemic toxicity was noted at 14 mg/kg/day for males and 19 mg/kg/day for females and above as histopathological changes in the liver. These observations included an increased incidence of hepatocytic (glycogen) pallor; the high dose animals also had increased incidence of fatty vacuolization (moderate or marked mid-zonar). High dose males had marked fine fatty periacinar, vacuolization and increased relative heart and liver weights. At 19 mg/kg/day and above, males had decreased absolute and relative kidney weights, while high dose females had increased relative kidney weights. Upon gross examination, there was an increased incidence of pale foci of the lungs of high dose animals and pale livers in the high dose males (external examination showed abdominal swelling). There was also an increased incidence of focal epithelialization of the alveolar walls of the lungs with associated macrophages. In addition, high dose females had reduced body weight gains. There was no evidence of carcinogenicity in either sex at the dose levels tested. For chronic toxicity, the NOEL was 3 mg/kg/day for males and 5 mg/kg/day for females and the LOEL was 14 mg/kg/day for males and 19 mg/kg/day for females based on histopathological changes in the liver.

e. Developmental Toxicity

In a developmental toxicity study (MRID# 00115248), albino rats of the Sim: (SD) FBR (Sprague Dawley derived) strain received by oral gavage either 0, 5, 25, or

150 mg/kg/day thiobencarb technical (97% a.i.) in Deionized Water/CMC/Tween 80 on days 6 through 19 of gestation. Maternal toxicity was observed as a treatment related decrease in body weight gains in the high dose group. There was no effect on food consumption; however, the high dose had lower food efficiency than the control group, an indicator of systemic toxicity. For maternal toxicity, the NOEL was 25 mg/kg/day and the LOEL was 150 mg/kg/day based on decreased body weight gains and decreased food efficiency. Developmental toxicity was noted as a slight increase in skeletal anomaly observations at the high dose mostly related to reduced ossification and an increase in runts in the high dose group. For developmental toxicity, the NOEL was 25 mg/kg/day and the LOEL was 150 mg/kg/day based on increased skeletal anomaly observations and an increase in the number of runts.

In another developmental toxicity study (MRID# 00164313), New Zealand white rabbits received 0, 20, 100, or 200 mg/kg/day technical thiobencarb (96.0% a.i,) by oral gavage from days 6 through 18 of gestation. Maternal toxicity was observed at 200 mg/kg/day as statistically significant increase in absolute and relative liver weights. For maternal toxicity, the NOEL was 100 mg/kg/day and the LOEL was 200 mg/kg/day based on increased liver weights. No developmental toxicity was observed at dose levels tested. For developmental toxicity, the NOEL was equal to or greater than 200 mg/kg/day and the LOEL was greater than 200 mg/kg/day. Based on the results of these studies, thiobencarb is not considered to be a developmental toxicant in rats or rabbits.

f. Reproductive Toxicity

In a multigeneration reproduction study (MRID# 40446201), Charles River CD rats received either 0, 2, 20, or 100 mg/kg/day Technical Bolero® (96.7% a.i.) by daily oral gavage in 0.5% CMC aqueous solution. Systemic toxicity was noted at 20 mg/kg/day and above based on enlargement of centrolobular hepatocytes (both generations) and hepatocyte single cell necrosis observed in both sexes of both generations including renal atrophic tubule consisting of regenerated epithelium. There were increased liver weights (absolute and relative) and increased kidney weights (absolute and relative) in the high dose group. There were also significant changes on body weights at 100 mg/kg/day and male kidney weights were increased in the high dose group. There were no effects on reproductive parameters. For Parental/Systemic toxicity, the NOEL was 2 mg/kg/day and the LOEL was 20 mg/kg/day based on histopathological changes of the liver and kidney. For reproductive toxicity, the NOEL was equal to or greater than 100 mg/kg/day and the LOEL was greater than 100 mg/kg/day.

g. Mutagenicity

Thiobencarb was evaluated in an Ames assay (MRID#s 00041174, 00084131 and 00135285) and was negative in tester strains TA100, TA98 and TA1537 at levels

up to 50 ug/plate, both with and without metabolic activation.

Thiobencarb was negative in a dominant lethal assay in mice (MRID# 00084133 and 00135282), administered at a single oral dose of 600 mg/kg and at an oral dose of 300 mg/kg for 5 days.

In a clastogenicity test in human lymphocytes (MRID# 40352401), thiobencarb (96.0% a.i.) was tested at dose levels of 0, 5, 10, and 20 ug/ml without S9 activation and at dose levels of 0, 10, 20, and 40 ug/ml with S9 activation. No mutagenic activity was noted.

In a micronucleus test in mice (MRID# 40352402), thiobencarb (96.0% a.i.) was tested at dose levels of 0, 270, 540, and 1080 mg/kg in males and at dose levels of 0, 405, 810, and 1620 mg/kg in females, as a single oral dose. A dose related increase in micronuclei was noted, and was statistically significant in high dose males and in the two highest doses in females. Four consecutive daily doses of 540 mg/kg caused statistically significant increases in the incidence of micronuclei in both sexes. This was considered as a positive mutagenic response.

, thiobencarb was shown to lack mutagenicity in three of the four mutagenicity tests conducted. No further testing is required at this time.

h. Metabolism

In a general metabolism study (MRID# 42340302), the disposition and metabolism of [Phenyl-U-^{14}C]-thiobencarb (Radiochemical Purity: not stated, but data in report, indicate acceptable purity of radiochemical; Specific Activity: 32.5 mCi/mmol prior to purification, specific activity following purification was not stated; Unlabeled Thiobencarb, (Purity: > 97.0%) was investigated in male and female Sprague-Dawley rats at a single low oral dose (30 mg/kg), repeated low oral doses (30 mg/kg x 14 days), and a single high dose (300 mg/kg). Thiobencarb was rapidly absorbed after oral administration as judged by the rate of excretion. No significant sex-related or dose group differences in absorption were noted. Excretion was relatively rapid at all doses tested, with a majority of radioactivity eliminated in the urine and feces by 48 hours. The extent of excretion was completed by 72 hours at the 300 mg/kg dose, but the mechanism responsible for this delay was not identified. No significant sex- or dose-related differences in urinary or fecal excretion of thiobencarb derived radioactivity were noted. Repeated low oral dosing did not affect elimination of thiobencarb in either male or female rats.

Fecal elimination of [Phenyl-U-^{14}C]-thiobencarb derived radioactivity was a minor route of excretion, and for urine, no significant sex- or dose-related differences in amount of radioactivity excreted by this route were observed. Residual levels of

thiobencarb derived radioactivity were also minor (less than 0.5% of an administered dose).

Urinary and fecal metabolites of [Phenyl-U-^{14}C]-Thiobencarb were isolated and identified by HPLC, TLC, and mass spectral analysis. The major metabolite detected was the glycine conjugate 4-chlorohippuric acid, comprising between 74-81% of an administered dose in urine. Other metabolites detected included 4-chlorobenzyl methyl sulfoxide and -sulfone, des-ethyl thiobencarb, and 4-chlorobenzoic acid, each representing less than 10% of an administered dose of thiobencarb. A single high or repeated low oral dose did not significantly affect the urinary or fecal metabolite profile for thiobencarb in male or female rats.

i. Neurotoxicity

Acute Neurotoxicity

In an acute neurotoxicity study (MRID# 42987001, 43148202), male and female Sprague-Dawley rats received a single oral administration of thiobencarb (96.9%) at doses of 0, 100, 500 or 1000 mg/kg. Neurobehavioral evaluations, consisting of Functional Observational Battery (FOB) and motor activity, were conducted at pre-study, Day 0, at time of peak effect (4 hrs post-dosing), Day 7 and Day 14. At Day 15, animals were euthanized and neuropathological examination performed on control and high-dose animals (5/dose/sex). With the exception of one high-dose female, which died on Day 3 of the study, all other animals survived until terminal sacrifice. An increased incidence of clinical signs, consisting of red deposits around the noses and mouths of high-dose animals, was noted. Gait abnormalities (rocking, lurching and swaying) were observed in some high-dose females. No significant differences were noted in either the mean body weight or body weight gain of any of the treated animals. Neurobehavioral evaluation revealed treatment-related FOB and motor activity findings at the mid- and high-dose levels. The effects were, in general, transient and observed only at the peak time of effect (4 hrs post-dosing). Although the incidences of FOB findings were not significantly different from control values, when taken together, a consistent, treatment-related pattern of neurobehavioral effects becomes clear. These findings included gait abnormalities (lurching, swaying and rocking), impaired mobility and decreased sensory responses (approach, touch, startle, tail pinch and pupil responses). In high-dose males, the startle response achieved statistical significance when measured at the time of peak effect. Hindlimb resistance was reduced in high-dose animals. Mean body temperature was significantly decreased in all treated males and mid- and high dose females. Total and ambulatory motor activity, measured at the peak time of effect on Day 0, showed significant treatment-related decreases in all mid- and high-dose animals. No treatment-related gross or neuropathological findings were present. Brain weights and measurements of the treated animals were comparable to control values. Thus, for systemic toxicity, the NOEL was 100 mg/kg/day and the LOEL was 500 mg/kg based on increased clinical signs and gait abnormalities. For

neurobehavioral toxicity, the NOEL was 100 mg/kg/day and the LOEL was 500 mg/kg based on gait abnormalities, decreased sensory responses, decreased body temperature and decreased motor activity.

Subchronic neurotoxicity

In a subchronic neurotoxicity study (MRID# 43001001), male and female Sprague-Dawley rats (10/sex/group) received oral administration of Bolero® 8EC at 0, 2, 20 or 100 mg/kg/day for 13 weeks. All animals survived until terminal sacrifice. Clinical signs were evident only within the first 4-hours post-dosing. During this time, there was an increased incidence of dried red material around the noses of all treated animals and dried tan or red material around the mouths of mid- and high-dose animals. Mean body weights and body weight gains of high-dose females were lower than controls. Food consumption was not affected by treatment. The absolute-and relative (to terminal body weight and brain weight) liver and kidney weights of high-dose males and females was statistically significantly increased. The relative (to the terminal body weight) liver weights of mid-dose males and the kidney weights of mid-dose females were statistically significantly increased. No clinical pathology was conducted. In addition, no treatment-related gross or neuropathological findings were present. Thus, for systemic toxicity, the NOEL was 2 mg/kg/day and the LOEL was 20 mg/kg/day based on increased clinical signs, decreased body weights, increased liver and kidney weights. For neurotoxicity, the NOEL was greater than 100 mg/kg/day (HDT) and a LOEL was not established.

j. Epidemiological Information

No cases of poisoning were located from any of the available databases on incidents related to the use of thiobencarb. EPA believes that this may be due partly to the relatively limited use of this chemical.

2. Toxicological Endpoints for Risk Assessment

a. Reference Dose (RfD)

The RfD/Peer Review Committee met on February 8, 1996, to discuss and evaluate the existing and/or recently submitted toxicology data in support of the thiobencarb reregistration and to reassess the RfD for this chemical.

The Committee recommended that the existing RfD for thiobencarb remain unchanged. The RfD for this chemical was based on the two year rat feeding study (MRID# 00154506) with a NOEL of 20 ppm (1 mg/kg/day). At the next higher dose level of 100 ppm (5mg/kg/day), decreased body weights and increased blood urea nitrogen levels were observed. An uncertainty factor of 100 was applied to account for both inter-species extrapolation and intra-species variability. On this basis, the RfD

was calculated by the Committee to be 0.01 mg/kg/day.

b. Carcinogenic Classification

The carcinogenic potential of thiobencarb was evaluated by the RfD/Peer Review Committee on February 8, 1996. The Committee considered the carcinogenicity phases of the combined chronic toxicity/carcinogenicity studies in rats (MRID# 00154506) and the carcinogenicity study in mice (MRID# 00086004) for carcinogenic classification.

The highest dose level tested in the rat (500 ppm, or 25 mg/kg/day) was considered to be adequate for carcinogenicity testing based on depression of cholinesterase activity and reduced body weight gain. The highest dose level tested in the mouse (1600 ppm, or 235 mg/kg/day in males and 302 mg/kg/day in females) was considered to be adequate based on body weight gain depression.

In rats, there was no treatment-related increase in tumors of any kind at any dose level. The Committee, therefore, concluded that the treatment did not alter the spontaneous tumor profile in this strain of rat.

In mice, adenomas and carcinomas of the harderian glands appeared to be increased in treated females (1, 2, 6, 5 and 7 tumors for the 0, 25, 10, 400 and 1600 ppm groups, respectively). However, the Committee noted several limitations with the study. First, the concurrent control incidence was lower than expected for females of this strain. This decreased incidence in the control group could possibly be due to chance and could not be precluded. Second, if a greater number of control mice had lived until completion of the study, more spontaneous tumors may have occurred, thus resulting in similar tumor incidence between treatment and control groups. Third, the study was carried out for 121 weeks, a significantly longer period than guideline requirements. Thus, the increased study length may have contributed to the appearance of tumors in treated females. Fourth, the Committee concluded that historical control incidence data from studies conducted for a significantly shorter duration should not be considered. The Committee reasoned that these shorter duration studies may not accurately depict tumor incidences because the tumor incidence would most likely be lower than what was observed in the studies used for carcinogenic classification. Thus, no historical control data were acceptable for review by the Committee.

On this basis, the Committee recommended that thiobencarb be classified as Group D chemical (not classifiable as to human carcinogenicity).

c. Other Toxicological Endpoints

On April 30, 1996, the Agency's Office of Pesticide Program Health Effects

Division Toxicity Endpoint Selection Committee (i.e. the TES Committee), met to discuss the toxicological endpoints to be used in various risk assessments for thiobencarb. A summary of the endpoints selected is provided in Table 2.

Dermal Absorption. In addition to the toxicological endpoints listed in Table 2, the TES Committee discussed the dermal absorption of thiobencarb.

Table 2. Summary of Toxicological Endpoints for Thiobencarb

TYPE OF EXPOSURE	NOEL	ENDPOINT
Acute Dietary (one day)	NOEL = 25 mg/kg/day established in a rat developmental toxicity study (MRID 00086873, 00093691 and 00115248)	Increases in incidence of reduced ossification and an increase in fetal runts.
Short-Term Occupational or Residential Exposure (one to seven days)	NOEL = 25 mg/kg/day established in a rat developmental toxicity study (MRID 00086873, 00093691 and 00115248).	Increases in the incidence of reduced ossification and an increase in fetal runts.
Intermediate-Term Occupational or Residential Exposure (one week to several months)	NOEL = 2 mg/kg/day for systemic toxicity established in a rat subchronic neurotoxicity study (MRID 430001001). This NOEL of 2 mg/kg/day is supported by a similar NOEL (2 mg/kg/day) established in the multigeneration reproduction study (MRID 40446201 and 409085701).	Histopathological changes in the liver and kidney.

In a dermal absorption study (MRID# 41215311), Sprague-Dawley® Crl:CD® (SD)BR male rats were dermally treated with either 0, 0.05, 0.5 or 5.0 mg/rat of ^{14}C-Thiobencarb (Radiochemical purity: 98.8%, Specific Activity: 359,092 dpm/ug) for exposure durations of 1, 2, 4, 10, or 24 hours (4 rats per dose per duration). The unlabeled compound used was Bolero® 8EC (Thiobencarb, Purity: 89% a.i.). This study may represent a worst-case scenario since the skin was washed approximately 1 hour prior to dosing rather than the recommended 24 hours (which would allow normal replacement of skin oils). Thus, this might tend to over-estimate absorption. Based on the results of the study, the Committee determined that thiobencarb is rapidly and

continuously absorbed at doses of 5.0, 46.8 and 498 ug/cm^2 for exposure times up to 24 hours. Absorption at 10 hours was 60.2, 52.6, and 17.1% for the 5.0, 46.8 and 498 ug/cm^2 dose groups, respectively. Maximum absorption at 24 hours was 71.5, 72.6, and 41.75 for the 5.0, 46.8 and 498 ug/cm^2 dose groups, respectively. Urine was the primary route of excretion.

On this basis, the committee recommended that a dermal absorption factor of 60.2%, observed at 10 hours in a dermal absorption study (MRID# 41215311), be used for risk assessment purposes.

3. Exposure Assessment

Thiobencarb, S-((4-chlorophenyl)methyl)N,N-diethylcarbamothioate, is a herbicide used on rice, lettuce, celery and endives. The herbicide is applied preemergence or early postemergence to control grasses and broadleaf weeds. Thiobencarb is applied using a variety of equipment including fixed-wing aircraft, helicopter, granular tractor-drawn spreader, and groundboom sprayer. Application rates vary from 4 to 8 lbs ai/acre depending on the formulation and the target crop.

There are four registered end-use products: Valent Bolero® 8 EC (EPA Reg. No. 59639-79), Valent Bolero® 10 G (EPA Reg. No. 59639-80), Bolero® 10 G (EPA Reg. No. 63588-5) and Bolero® 8 EC (63588-6). Thus, the following exposure assessment is based on these products.

EPA expects both dietary (i.e. food and drinking water sources) and occupational exposure from the use of thiobencarb (there are no residential uses). Dietary exposure is expected to be both acute and chronic (i.e. one day and over a long-term period of time). Occupational exposure is expected to occur over a short to intermediate term (i.e. from one day to several months).

a. Dietary Exposure from Foods Sources

Regulatory Background

EPA completed the Thiobencarb Phase 4 Review on 4/15/91. A Thiobencarb Data-Call-In (DCI) Notice was subsequently issued 8/13/91. HED has conducted Phase 5 Reviews of several residue chemistry studies that were submitted in response to the DCI as well as studies that were deemed acceptable during Phase 4 Review. Based on the available data, a risk assessment can be performed for this chemical.

Tolerances for residues of thiobencarb in/on plant and animal commodities [40 CFR §180.401(a) and (b)] are expressed in terms of the combined residues of thiobencarb and its chlorobenzyl and chlorophenyl moiety-containing metabolites. Primary metabolites of interest are: 4-Chlorobenzylmethylsulfone, 4-Chlorobenzoic acid, N-(4-

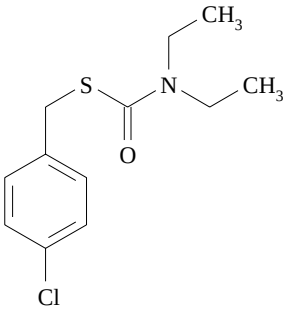
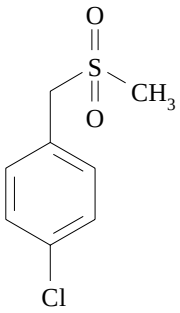
Chlorobenzoyl)glycine, and 4-Chlorobenzylthio conjugates. Provided in Table 3 is the chemical structure of thiobencarb and the structures of its primary metabolites. Tolerances are established under 40 CFR §180.401(a) for: rice, grain at 0.2 ppm; rice, straw at 1.0 ppm; meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep at 0.2 ppm; eggs at 0.2 ppm; and milk at 0.05 ppm. Tolerances with regional registration, in accordance with 40 CFR §180.1(n), are established under 40 CFR §180.401(b) for celery, endive (escarole), and lettuce at 0.2 ppm each. Adequate methods are available for the enforcement of established tolerances.

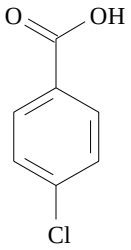
Summary of Science Findings

i. Directions for Use

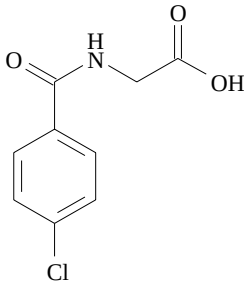
A REFS search conducted 10/18/95 identified four thiobencarb end-use products (EPs) registered to Valent U.S.A. Corporation and K-I Chemical U.S.A., Inc. under FIFRA Section 3 (as noted above), and 17 active SLNs registered under FIFRA Section 24(c) for use on food/feed crops. A list of thiobencarb EPs is presented below in Table 4.

Table 3. Chemical structures of thiobencarb and its metabolites containing the chlorobenzyl and chlorophenyl moiety

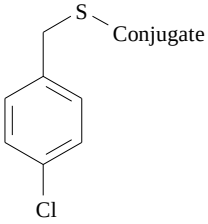
Compound: Chemical name	**Compound**: Chemical name
	
Thiobencarb S-((4-Chlorophenyl)methyl)diethylcarbamothioate	4-Chlorobenzylmethylsulfone



4-Chlorobenzoic acid



N-(4-Chlorobenzoyl)glycine



4-Chlorobenzylthio conjugates

Table 4. Thiobencarb end-use products (EPs) with food/feed uses registered to Valent U.S.A. Corporation and K-I Chemical U.S.A., Inc.

EPA Reg. No.	Acceptance Date	Formulation	Product Name
EPs Registered to Valent U.S.A. Corporation			
59639-79 [1]	4/20/94	8 lb/gal EC	Bolero® 8EC (Herbicide)
59639-80 [2]	11/29/93	10% G	Bolero® 10 G (Herbicide)
EPs Registered to K-I Chemical U.S.A Inc.			
63588-5	2/94	10% G	Bolero® 10 G
63588-6	2/94	8 lb/gal EC	Bolero® 8EC

[1] EPA Reg. No 59639-79 is the parent label for the following Section 24(c) registrations: AR940002, AR940003, AR950004, CA930003, FL910003, FL930010, LA950005, MO930007, MO940005, MO950002, MS930009, MS930010, MS950007, and TX930023.

[2] EPA Reg. No. 59639-80 is the parent label for the following Section 24(c) registrations: AR940001, MS930011, and TX930024.

A comprehensive summary of registered food/feed use patterns for thiobencarb, based on the products registered to Valent U.S.A. Corporation, and all active SLN registrations is presented in Appendix 2. For the purposes of reregistration, label amendments are required for Valent's end-use products (EPA Reg. Nos. 59639-79 and 59639-80) to specify a 14-day water holding interval following thiobencarb application to rice fields. Additionally, the following use restrictions should be added to thiobencarb labels: "Do not use on rice paddies where commercial catfish or crayfish farming is practiced. Do not use adjacent to catfish or crayfish ponds."

A tabular summary of the residue chemistry science assessments for reregistration of thiobencarb is presented in Appendix 3. The conclusions listed in Appendix 3 regarding the reregistration eligibility of thiobencarb are based on the use patterns registered by the basic producer. All end-use product labels (e.g., MAI labels, SLNs, and products subject to the generic data exemption) must be amended such that they are consistent with the basic producer labels.

ii. Plant Metabolism

The qualitative nature of the residue in plants is adequately understood based on an acceptable study depicting the metabolism of thiobencarb in rice. On May 13, 1993, the HED Metabolism Committee determined that the current tolerance expression for residues of thiobencarb and its metabolites containing the chlorobenzyl and chlorophenyl moieties is

appropriate.

iii. Animal Metabolism

For the purposes of reregistration and risk assessment, the qualitative nature of the residue in animals is adequately understood based on acceptable studies conducted on ruminants and in poultry. The residue of concern in eggs, milk, and poultry and livestock tissues include the parent thiobencarb and its metabolites containing the chlorobenzyl and chlorophenyl moieties. The current tolerance expression for animal commodities, as defined in 40 CFR §180.401(a), is adequate.

iv. Residue Analytical Methods - Plants and Animals

The requirements for residue analytical methods are fulfilled for the purposes of reregistration. Adequate methods are available for enforcement and data collection purposes for both plant and animal commodities. Successful radiovalidation of the enforcement methods, using samples from the metabolism studies, has also been conducted. The 1/94 FDA PESTDATA database indicates that residues of thiobencarb are completely recovered (>80%) using multiresidue method Section 302 (Luke method; Protocol D), and variably recovered using method Section 304 (Mills, Onley, Gaither method; fatty food). The registrant has conducted multiresidue method trials with thiobencarb metabolites 4-chlorobenzylmethylsulfone and 4-chlorobenzylmethylsulfoxide using Protocol E and with 4-chlorobenzoic acid using Protocol B. HED has forwarded the results of these multiresidue trials to FDA for evaluation and inclusion in PAM Vol. I, Appendix I.

v. Storage Stability

Adequate storage stability data are available to support the established tolerances. Acceptable storage stability studies have been submitted for representative plant and animal commodities. The available plant and animal metabolism studies are also validated by adequate storage stability data.

vi. Magnitude of the Residue in Plants

The reregistration requirements for magnitude of the residue in/on plants are fulfilled for the following commodities: celery, endive, lettuce, and rice grain and straw. No additional data are required. Adequate field trial data, following treatments according to the maximum registered use patterns, have been submitted for the commodities listed above. The available data were submitted in conjunction with tolerance petitions for celery, endive, and lettuce (PP#5F3158), and rice grain and straw (PP#0F2322, 5G1582, 6F1763, and 2G1231), and are adequate to support reregistration requirements including tolerance reassessment.

vii. Magnitude of the Residue in Processed Food/Feed

The reregistration requirements for magnitude of the residue in the processed food/feed commodities of rice are fulfilled. An acceptable study depicting the potential for thiobencarb residues of concern to concentrate in rice processed fractions has been submitted and evaluated. The data indicate that the combined residues of thiobencarb and 4-chlorobenzylmethylsulfone did not concentrate in polished rice and bran processed from rice samples that received postemergence application of the registered 10% G formulation at an exaggerated rate (5x); however, the combined residues concentrated 2x in hulls. Although residue concentration was observed in hulls, the observed combined residues of thiobencarb and its metabolite (<0.06 ppm) in/on hulls following exaggerated rate treatment were below the established tolerance of 0.2 ppm for rice grain.

viii. Magnitude of the Residue in Meat, Milk, Poultry, and Eggs

The reregistration requirements for magnitude of the residue in milk and livestock tissues as well as in eggs and poultry tissues are fulfilled. There are no registered direct animal treatments of thiobencarb on cattle, goats, hogs, horses, poultry, or sheep.

The available dairy cattle and poultry feeding studies indicates that the combined residues of thiobencarb and its metabolites [4-chlorobenzoic acid, 4-chlorobenzyl-methylsulfone, and 4-chlorobenzylmethylsulfoxide] will not exceed the established tolerances.

ix. Magnitude of the Residue in Potable Water

The reregistration requirements for magnitude of the residue in water will be considered fulfilled when revisions are made to Valent's end-use product labels (EPA Reg. Nos. 59639-79 and 59639-80) to prohibit use of treated water for livestock watering or for drinking or irrigation for a specified time period after treatment. Based on the results of an acceptable magnitude of residue in potable water study (MRIDs 43404003, 43404004, and 43404005), thiobencarb and thiobencarbsulfoxide residues in runoff and receiving waters associated with rice fields did not fall to acceptable levels until 14 days after treatment. Thus, HED has determined that a 14-day water holding interval should be imposed following thiobencarb application to rice fields at the maximum registered rate. If the registrant does not wish to institute this label restriction, then a irrigated crop field trial and a drinking water intake study will be required.

The use of the thiobencarb granular formulation (Bolero® 10G, EPA Reg. No. 59639-80) in California is regulated under the Basin Plan for the Sacramento River Basin established by the California Regional Water Quality Control Board, Central Valley Region. A performance goal of 1.5 ppb is strictly monitored, and growers must adhere to a program of approved management practices, including a 30-day water holding restriction.

x. Nature and Magnitude of the Residue in Fish

The reregistration requirements for nature and magnitude of the residue in fish will be fulfilled when label revisions are made on Valent's end-use products (EPA Reg. Nos. 59639-79 and 59639-80) to specify the following use restrictions: "Do not use on rice paddies where commercial catfish or crayfish farming is practiced. Do not use adjacent to catfish or crayfish ponds."

xi. Magnitude of the Residue in Irrigated Crops

Data depicting the magnitude of the residue in irrigated crops are not required for reregistration purposes since the Agency is imposing a 14-day water holding interval.

xii. Magnitude of the Residue in Food-Handling Establishments

Thiobencarb is not registered for use in food-handling establishments; therefore, no residue chemistry data are required under this guideline topic.

xiii. Confined/Field Rotational Crops

Valent's thiobencarb end-use labels specify a 6-month plantback interval following rice and all other crops, except celery, endive and lettuce for which rotational crop plant-back intervals are 4-months. These currently specified plant-back intervals are appropriate.

xiv. Residue Information (for dietary risk assessment)

Tolerances for thiobencarb are published in 40 CFR 180.401(a) and (b). Tolerances have been established for rice grain at 0.2 ppm; meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep at 0.2 ppm; eggs at 0.2 ppm; and milk at 0.5 ppm. Tolerances with regional registrations are established for celery, endive, and lettuce at 0.2 ppm each. Tolerance level residues and 100 percent crop treated assumptions were made for all commodities. Anticipated residue information was not used for this analysis.

A summary of the residue information that was used in the dietary risk assessment is provided in Table 1 of Appendix 5.

b. Dietary Exposure from Drinking Water

Thiobencarb is not currently regulated under the Safe Drinking Water Act. Public water supply systems are not required to sample and analyze for thiobencarb. Thus, no maximum contaminant level (MCL) is established for thiobencarb in drinking water systems. An MCL is an action level as established by the EPA Office of Water to ensure the safety of drinking water. In addition, the lifetime Health Advisory (HA) for thiobencarb has not been

established. Estimates of thiobencarb concentrations in well, ground water and surface water were prepared by the EFED.

Ground Water

Limited groundwater monitoring information is available for thiobencarb. The "Pesticide in Ground Water Database" (Hoheisel et al., 1992) reported sampling for thiobencarb in 270 wells in California and 65 wells in Missouri. Two detections of thiobencarb in ground water were reported in Missouri and at very low concentrations (0.2 - 0.3 ppb). However, no limit of detection (LOD) or limit of quantification (LOQ) were provided to normalize the data for non-detectable residues. This is an important consideration since thiobencarb was not detected in almost all wells sampled. Therefore, the groundwater sampling data are not usable for drinking water risk assessment purposes.

Surface Water

Thiobencarb has the potential to contaminate surface water from releases of rice paddy water following thiobencarb applications or from spray drift associated with aerial or ground spray application to other registered sites. EFED provided estimates of thiobencarb residues in surface water by utilizing the Generic Estimated Environmental Concentration program (GENEEC) to estimate aquatic EEC (Estimated Environmental Concentrations) of thiobencarb on celery, lettuce, and endive (but not rice) and from the EPA Office of Water's STORET database. In addition, results of a thiobencarb surface water monitoring studies in California (USEPA, 1997) are also available. The results of these data are provided below.

GENEEC model

The GENEEC model was used to estimate aquatic EEC concentrations for the thiobencarb lettuce, endive and celery uses (aquatic EEC concentration modeling for rice was not conducted because the Agency does not have a computer simulation model which will estimate concentrations for this use). The range of aquatic EECs was 140 mg/L (1.4×10^5 ppb) for 6 lb a.i. application rate and 180 mg/L (1.8×10^5 ppb) for the 8 lb a.i. application rate. Thiobencarb is expected to dissipate in pond water at an approximate rate of 0.4 - 0.6 mg/L/day (400 - 600 ppb/day). However, since GENEEC cannot model rice scenarios (almost 95% of all thiobencarb use is on rice), these exposure estimates are not applicable to most thiobencarb uses.

STORET database

Detection of thiobencarb was identified in eight states: California, Georgia, Maryland, North Carolina, Oregon, Oklahoma, Texas and Washington. However, detection of thiobencarb was only observed in two states where

thiobencarb is used on rice, California and Texas. Thirty-nine positive detections were reported for 3,130 samples (approximately 1%) with a maximum concentration of 0.24 mg/L (240 ppb) and a mean concentration of 0.10 mg/L (100 ppb). Similar to the groundwater monitoring data discussed above, no LOD or LOQ were provided to normalize the STORET data for non-detectable residues. Therefore, the STORET data are not applicable for drinking water risk assessment purposes.

California Surface Water Monitoring data

Monitoring for residues of specific rice pesticides in surface water of California's Sacramento River basin was performed by the California Environmental Protection Agency (CAL EPA), sometimes in conjunction with the California Rice Industry Association, from 1993 to 1996. HED estimates that the City of Sacramento is the only locality in the US rice growing region relying on surfacewater as its source of drinking water (i.e. the city utilizes the Sacramento River as its source of drinking water).

In 1993, 17 samples were collected just before the intake to the Sacramento River drinking water treatment facility (the only year of the four year study that samples from this location were collected). No detections above a limit of detection of 0.1 ug/L were reported. However in 1993, due to substantial flow in the Sacramento River, water was diverted south of the sampling location via the Yolo Bypass. Thus, diverting water from the Sacramento River drinking water treatment facility may have contributed to thiobencarb levels below the limit of detection. Therefore, HED concludes that even though thiobencarb residues at the Sacramento River were below the limit of detection (0.1 ug/L), thiobencarb residues may be higher if water was not diverted via the Yolo Bypass.

c. Occupational Exposure

An occupational and/or residential exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete.

In the case of thiobencarb, EPA has determined that there is a toxicological concern and there is potential exposure to mixers, loaders, applicators, or other handlers during activities that would occur under the usual thiobencarb use scenarios. Also, there is potential exposure to persons reentering sites that have been treated with thiobencarb. Therefore, the Agency has assessed application and post-application exposure to thiobencarb.

At this time, products containing thiobencarb are intended primarily for occupational uses

only and not for homeowner uses. Thus, this exposure assessment is limited to occupational uses only. Further, EPA expects that, based on the use patterns, exposure to thiobencarb will occur for a short to intermediate duration; chronic exposure is not expected. Finally, the Agency expects exposure to occur via the dermal and inhalation routes.

i. Handler Exposure

EPA has identified eight major exposure scenarios from the use patterns of thiobencarb for its occupational exposure assessment: (1a) mixing/loading liquids for aerial application; (1b) mixing/loading liquids for groundboom application; (2a) loading granulars for fixed-wing aircraft; (2b) loading granulars for tractor-drawn spreader application; (3) applying sprays with a fixed-wing aircraft; (4) applying granulars with a fixed-wing aircraft; (5) applying sprays with a helicopter; (6) applying granulars with a tractor-drawn spreader; (7) applying sprays with groundboom equipment; and, (8) flagging aerial spray applications.

Potential dermal and inhalation baseline unit exposure (which are derived from PHED V. 1.1), along with corresponding calculated daily exposures, are presented in Table 5. No chemical-specific data were submitted. Baseline unit exposure is the PHED exposure estimate with just the clothing scenario that was provided in the PHED data base (i.e. the baseline clothing). Dermal exposure is several orders of magnitude greater than inhalation exposure.

Potential daily exposure is calculated using the following formula:

Daily exposure (mg ai /day) = Unit exp. (mg ai/lb ai) x Max. App. Rate (lb ai/ac) x Max. Area Trt. (ac/day)

Provided in Appendix 4 are the caveats, parameters and assumptions specific to each exposure scenario.

ii. Post-Application Exposure

Based on the use patterns of thiobencarb, EPA has determined that there is potential exposure for persons entering treated sites after application is complete. Workers may be entering treated areas to perform such tasks as scouting, thinning, hoeing or harvesting. However, there are no chemical-specific data available upon which to assess the risks from post-application exposures.

4. Risk Assessment

EPA expects both dietary and occupational exposure from the use of thiobencarb (there are no residential uses). Dietary exposure occurs via the oral route while occupational exposure occurs via the dermal and inhalation routes. An inhalation risk assessment is not required since the LC_{50} of > 42.8 mg/L hour in an acute inhalation study placed thiobencarb in Toxicity Category IV.

Table 5. Thiobencarb Baseline Unit Exposures and Daily Exposures (Short and Intermediate-Term)

Exposure Scenario (Number)	Crop	Baseline Dermal Unit Exposure (mg/lb ai)[a]	Baseline Inhalation Unit Exposure (ug/lb ai)[b]	Application Rate (lb ai/acre)[c]	Daily Acres Treated[d]	Daily Absorbed Dermal Exposure (mg/day)[e]	Daily Inhalation Exposure (mg/day)[f]
Mixer/Loader Exposure							
Mixing/Loading Liquids for Aerial Application (1a)	Rice	2.9	1.2	4	350	2444.1	1.68
Mixing/Loading Liquids for Groundboom Application (1b)	Rice			4	80	558.7	0.38
	Endive/Lettuce			6		838.0	0.58
	Celery			8		1,117.3	0.77
Loading Granulars for Fixed-wing Aircraft Application (2a)	Rice	0.0076	1.7	4	350	6.6	2.3
Loading Granulars for Tractor-drawn Spreader Application (2b)	Rice				80	1.5	0.54
Applicator Exposure							
Applying Sprays with a Fixed-wing Aircraft (Enclosed Cockpit) (3)	Rice	See Eng. Controls	See Eng. Controls	4	350	See Eng. Controls	See Eng. Controls
Applying Granulars with a Fixed-wing Aircraft (Enclosed Cockpit) (4)	Rice	See Eng. Controls	See Eng. Controls	4	350	See Eng. Controls	See Eng. Controls
Applying Sprays with a Helicopter (Enclosed Cockpit) (5)	Rice	See Eng. Controls	See Eng. Controls	4	350	See Eng. Controls	See Eng. Controls
Applying Granulars with a Tractor-Drawn Spreader (Enclosed Cab) (6)	Rice	See Eng. Controls	See Eng. Controls	4	80	See Eng. Controls	See Eng. Controls
Applying Sprays with a Groundboom Sprayer (7)	Rice	0.015	0.7	4	80	2.9	0.22
	Endive/Lettuce			6		4.3	0.34
	Celery			8		5.8	0.45
Flagger Exposure							
Flagging Spray Applications (8)	Rice	0.01	0.28	4	350	8.4	0.39

a Baseline dermal unit exposure represents long pants, long sleeve shirt, no gloves, open mixing/loading, and open cab tractor. Baseline data are not available for aerial application and granular applications with a tractor-drawn spreader.

b Baseline inhalation exposure represents no respirator.

c Application rates are the maximum found in the thiobencarb labels [EPA Reg. Nos. 59639-79 and 59639-80].

d Daily acres treated are from EPA OREB estimates of acreage that could be treated in a single day for each exposure scenario of concern.

e Daily absorbed dermal exposure (mg/day) = Exposure (mg/lb ai) * Appl. rate (lb ai/A) * Acres Treated * Dermal Absorption Rate (60.2%)

f Daily inhalation exposure (mg/day) = Exposure (ug/lb ai) * (1mg/1000 ug)conversion * Appl. Rate (lb ai/A) * Acres Treated

Dietary exposure (food and drinking water sources) is expected to occur over an acute through chronic period. To assess the acute dietary risk, EPA calculates a margin of exposure (MOE), which is the ratio of the NOEL to exposure. To assess chronic risk, EPA calculated the percent of the reference dose [RfD] (i.e. % RfD) used.

a. Dietary Risk

i. Acute Dietary (Food Source) Risk

The Dietary Risk Evaluation System (DRES) acute analysis estimates the distribution of single-day exposure for the overall U.S. population and certain subgroups. It includes all published uses of thiobencarb, even those commodities that are being recommended for revocation. The analysis evaluates individual food consumption as reported by respondents in the USDA 1977-1978 Nationwide Food Consumption Survey and accumulates exposure to the chemical for each commodity.

The MOE is calculated by dividing the acute dietary NOEL (i.e. mg/kg/day) by the high-end exposure (see Table 1 of Appendix 5 for the exposure estimates). Because the endpoint of concern for acute dietary risk assessment is a developmental toxicity effect, the only subgroup of concern is females (13+ years). Generally, acute aggregated MOEs greater than 100 tend to cause no dietary concern when the data are compared to a toxicological endpoint from an animal study (such is the case for thiobencarb). Since the only subgroup of concern is females (13+) and represents an MOE = 8928 (as represented in Table 3 of Appendix 5), HED is not concerned with acute dietary risks from exposure to thiobencarb residues in food.

ii. Acute Dietary (Drinking Water) Risk

Due to limitations with available groundwater sampling data, no groundwater data are applicable for risk assessment purposes. Even though there is an absence of applicable groundwater data, based on the environmental fate of thiobencarb and the soil profile of rice fields, HED does not believe that thiobencarb would be a concern to groundwater. First, thiobencarb is slightly persistent in water, generally not very mobile, tends to bind to soil organic matter, and doesn't desorb. Second, rice fields are usually underlain by a clay layer to restrict water movement through the soil and help contain the water in the flooded field. This clay layer will significantly limit the amount of leaching that occurs in rice fields (U.S.EPA, 1996g).

As noted above, approximately 95% of thiobencarb applications are made to rice. In addition, HED estimates that the City of Sacramento is the only locality in the US rice growing region utilizing surface water as its drinking water. Data from the California surface water monitoring study indicated thiobencarb residues were not above a limit of detection of 0.1 ug/L (0.1 ppb). Thus, drinking water exposure was calculated using the following formula:

Exposure (mg/kg/day) = (ppb thiobencarb in the water consumed)(10^{-6})(22.6)

Thus, drinking water exposure = 2.26×10^{-6} mg/kg/day and a resulting MOE > 10,000. Therefore, HED is not concerned with acute drinking water risks from exposure to thiobencarb residues in drinking water.

Water consumption is defined as all water obtained from the household tap that is consumed either directly as a beverage or is used to prepare foods (mixing water with a can of soup) and beverages (diluting frozen juice concentrate). Two generally accepted default values for water consumption are 2 liters per day (28.6 g/kg-body wt/day) or 1.5 liters per day (21.4 g/kg-body wt/day. The 22.6 g/kg-body wt/day used in this calculation was derived using water consumption values and self-reported body-weights obtained from USDA's 1977-1978 Nationwide Food Consumption Survey.

iii. Total Acute Dietary (Food Sources and Drinking Water)

To assess total acute dietary exposure and MOEs, the following formulas were utilized:

Total acute dietary exposure = acute food source exp. (high end exp.) [mg/kg/day] + drinking water exp. (high end exp.) [mg/kg/day]

Total acute dietary MOE= NOEL (mg/kg/day) / total acute dietary exposure (mg/kg/day)

Food source exposure (high end exposure) was 0.0028 mg/kg/day based on the high end exposure for females (13+ years) (Appendix 5; Table 3). Drinking water exposure (high end exposure) was 2.26×10^{-6} mg/kg/day based on surface water exposure as discussed previously. Thus, the total acute dietary MOE is 8846. Therefore, HED is not concerned with total acute dietary risks from exposure to thiobencarb.

iii. Chronic Dietary (Food Source) Risk

A DRES chronic exposure analysis was performed using tolerance level residues and a 100 percent crop treated assumption to estimate the Theoretical Maximum Residue Contribution (TMRC) for the general population and 22 subgroups. A summary of the TMRCs and the % RfD values for the U.S. general population, non-nursing infants (<1 year old) children (1-6 years) and females (13+ years) are provided in Table 2 of Appendix 5. The chronic analysis for thiobencarb is a worst case estimate of dietary exposure with all residues at tolerance level and 100 percent of the commodities assumed to be treated with thiobencarb.

As shown in Table 6, much less than 100% of the RfD is occupied by the dietary uses recommended through reregistration. Existing tolerances result in a TMRC which represents 12.8% of the RfD for the U.S. general population. The highest subgroup, Non-Nursing Infants (<1 year old), occupies 42.9% of the RfD. In addition, numerous conservative assumptions have been considered into this assessment. Thus, the actual % RfD is considered $\leq$ 42.9%. Therefore, HED is not concerned with chronic dietary risks from exposure to thiobencarb residues in food.

Table 6. Chronic Dietary (Food Source) Risk Evaluation for Thiobencarb

POPULATION SUBGROUP	Exposure (mg/kg/day)	%RfD (Chronic - noncancer)
General U.S. Population	0.001280	12.8
Non-nursing infants (< 1 year)	0.004294	42.9
Children (1-6 years)	0.002945	29.5
Females (13 + years)	0.001103	11.03

iv. Chronic Drinking Water Risk

As noted previously, due to limitations with available groundwater sampling data, no groundwater data are applicable for risk assessment purposes. However, even though there is an absence of applicable groundwater data, based on the environmental fate of thiobencarb and the soil profile of rice fields, HED does not believe that thiobencarb would be a concern to groundwater.

HED utilized data from the California surface water monitoring study to access chronic drinking water exposure. A drinking water exposure estimate of 0.1 ug/L (2.26×10^{-6} mg/kg/day) was used to assess chronic exposure (as was performed for acute drinking water exposure) since this is the only data available. Thus, high end drinking water exposure was utilized for the chronic drinking water risk assessment. This corresponds to a %RfD = 0.23. Therefore, HED is not concerned with chronic drinking water risks from exposure to thiobencarb in drinking water.

v. Total Chronic Dietary (Food Sources and Water) Risk

To assess total chronic dietary exposure and MOEs, the following formulas were utilized:

Total chronic dietary exposure (mg/kg/day) = food source chronic exp. (average exp.) [mg/kg/day] + drinking water exp. high end exp. *) [mg/kg/day]

$$\%\ RfD = \frac{\text{total chronic dietary exposure (mg/kg/day)}}{\text{RfD (mg/kg/day)}}$$

* High end exposure was used due to a lack of average exposure data.

Thus, this represents a percent RfD = 43.2%. Therefore, EPA is not concerned with total chronic dietary risks from exposure to thiobencarb.

vi. Dietary (food source and water) Carcinogenic Risk

Since thiobencarb is a Group D carcinogen (not classifiable as to human carcinogenicity), a dietary carcinogenic risk assessment is not required.

b. Occupational Risk

i. Handlers

The short-term and intermediate-term MOEs for thiobencarb calculated from Baseline and Risk Mitigation unit exposures are provided in Tables 7 and 8. Two types of risk mitigation were evaluated: (1) adding personal protective equipment (PPE) to the baseline clothing: and (2) instituting engineering controls (e.g. closed system). The unit exposure values for PPE and Engineering Controls are from PHED. As noted previously, a inhalation exposure assessment is not required since the LC_{50} of > 42.8 mg/L/1 hour in an acute inhalation study placed thiobencarb in Toxicity Category IV. Provided in Appendix 4 are the assumptions used for these calculations.

The daily dermal dose is calculated using a 60 kg body weight for short-term exposure and a 70 kg body weight for intermediate-term exposure. A 60 kg body weight is used for short-term exposure because this exposure is based on a developmental toxicity endpoint. The following formula was used to calculate the daily dermal dose:

Daily Dermal Dose (mg ai/kg/day) = Daily Dermal Exp. (mg ai/day) x 1/Body weight (kg) x 60.2% dermal absorption

These calculations of daily dermal dose of thiobencarb received by handlers are used to assess the dermal risk to those handlers. The short-term dermal MOEs were calculated using a dermal absorption rate of 60.2 percent and a NOEL of 25 mg/kg/day. The intermediate-term dermal MOEs were calculated using a dermal absorption rate of 60.2 percent and a NOEL of 2 mg/kg/day. The following formula was used for MOE calculations:

MOE = NOEL (mg/kg/day)/Daily Dermal Dose (mg/kg/day)

Short-term

EPA generally considers a MOE for occupational exposures of 100 to be protective of human health. The calculations of short-term risk estimates indicate that the MOEs are greater than 100 at **baseline** for the following scenarios:

- (2a) loading granulars for fixed-wing aircraft application;
- (2b) loading granulars for tractor drawn spreader application;
- (7) applying sprays with a groundboom sprayer; and,
- (8) flagging liquid aerial application.