PMSD/ISB

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

JUN 27 1988

EXPEDITE

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Memorandum

Subject: Acephate; Residue data in support of a dietary exposure assessment; Record No. 223409; RCB No. 3944.

From: Francis B. Suhre, Chemist
Special Registration Section II
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

Thru: Edward Zager, Section Head
Special Registration Section II
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

To: John Tice, PM-16
Insecticide-Rodenticide Branch
Registration Division (TS-767)

This review is being expedited at the request of Edwin F. Tinsworth, Director, Registration Division.

RD requested that RCB review residue data, generated in support of a dietary exposure assessment for acephate/methamidophos. These data were submitted by Chevron Chemical Co. in response to issues raised in a May 6, 1988, meeting with TOX Branch.

Acephate, O,S-dimethyl acetyl phosphoramidothioate, is a systemic organophosphate insecticide manufactured by Chevon Chemical Co.; Chevron markets acephate under the tradename ORTHENE.

Tolerances are established (40 CFR 180.108) for residues of the insecticide acephate and its cholinesterase inhibiting metabolite O,S-dimethyl phosphoramidothioate (methamidophos).

A Registration Standard Guidance Package for acephate was issued September 1987. As stated in that document, the metabolic nature of acephate in plants and animals is adequately understood; the residues of concern are acephate, per se, and its metabolite, methamidophos.

Analytical Method RM-12A (GC/thermionic detection) is adequate for the enforcement of established tolerances. Method RM-12A is described in PAM-II as Method 1 for acephate.

RCB's files indicate at least 3 dietary exposure assessments have been conducted for residues of acephate/methamidophos:

1. Task 4: Exposure Profile (see attachment #1); conducted in conjunction with the Residue Chemistry Chapter of the Acephate Registration Standard. This dietary exposure assessment utilized established tolerances (1982) and food factors to determine a Theoretical Maximum Residue Concentration (TMRC). According to this assessment 4 food items contributed 86.6% of the TMRC, as follows: beans (21.6%), celery (10.1%), lettuce (44.8%), and milk/dairy products (10.1%).

2. RCB expedited review (W. Hazel, memo of 5-14-85; see attachment # 2). This review considered potential reduction of acephate/methamidophos residues resulting from processing and or cooking of raw agricultural commodity after harvest. A TAS analysis was conducted to determine each food item's contribution to the Allowable Daily Intake (ADI). Apples and citrus were included in the TAS analysis because a temporary tolerance for apples was established and a temporary tolerance for citrus was pending at that time. Results of the TAS analysis indicated contributions of >1% of the ADI from: celery, lettuce, green succulent beans, dried beans (pinto and navy), soybean defatted flour and oil, citrus pulp, fresh apples and juice, and milk (nonfat solids, fat solids, and sugar (lactose)). Based the limited data available, RCB concluded that trimming, washing, cooking and or canning of fresh vegetables, and commercial processing of soybeans will result in some reduction (less than an order of magnitude) of acephate/methamidophos residues, however, the available data do not allow for estimating the extent of residue reduction associated with each RAC as it undergoes additional processing and or cooking after harvest.

3. SIS memo (K. Barbehenn, memo dated 5-21-87; see attachment # 3). This dietary assessment utilized field residue data as opposed to tolerance residues, and took into account the percent of crop treated. Using this approach, the estimated dietary exposure to acephate residues was reduced by 75 %.

In this submission (Record No. 223409) Chevron Chemical Co. provided several summary data Tables (1-5), as follows:

Table 1: Established tolerances accounting for >70% of the TMRC (See Acephate Registration Standard, Residue Chemistry Task 4) are compared with the actual residue levels found (source of data not specified). All values are reported in ppm.

commodity	Established Tolerances	Average Residue	Highest Residue found
Beans (dry and succulent)	3	0.54	2.04
Celery	10	1.69	4.82
Lettuce (head)	10	0.80	5.12
Lettuce (leaf)	10		

Table 2: Proposed tolerances (accounting for >85% of the TMRC from pending tolerances) are compared with actual residues (source not specified) for the same commodities. All values reported in ppm.

Fruit commodity	Proposed Tolerances	Average Residue	Highest Residue found
Apples	2	0.10	0.50
Cabbage	5	0.72	1.38
Citrus	3	0.48	2.60
Cucumber	5	1.22	4.20
Melons	5	1.88	5.30
Tomatoes	4	1.0	3.70

Table 3: Established tolerances are compared to average residues (source of data not specified) found in or on fresh and processed fractions. All values are reported in ppm.

Crop	Average Residue	Tolerance
<u>Lettuce</u>		10
Whole plant[a]	3.0	
Head[b]	2.6	
Field packed	0.94	
Head[c]	1.5	

a. One damaged leaf removed.
b. Plus 10 wrapper leaves.
c. Plus cap leaf.

Mint Hay		15
Green hay	2.6	
Mint oil	0.0	
Spent hay	0.31	
Soybeans		1
Beans		1
Oil		4
Meal		
Snap Beans		3
Fresh at harvest	0.34	
Fresh at processing	0.16	
Fresh at market	0.12	
Canned	0.07	
Frozen	0.03	
Lima Beans		3
Mature pods and beans	1.15	
Shelled beans	0.47	
Dry shelled beans	0.09	

Table 4: Acephate residue data from FDA monitoring surveys (1978-1985) are summarized and compared to established tolerances. All values are in ppm.

Crop	Number of samples	Average residue	Highest Residue	Tolerance
Lettuce	217	0.2	3.52	10
Beans	63	0.22	2.19	3
Peppers	364	0.55	5.17	4

Table 5: Residue data from Chevron's market basket survey (1984-1985) are summarized and compared to established tolerances. All values are reported in ppm.

Crop	Average residue	Highest Residue	Tolerance
Celery	0.02	0.08	10.0
Lettuce	0.02	0.11	10.0
Peppers	0.14	0.98	4.0
Beans (snap)	0.01	0.03	3.0

RCB's Conclusions

1. Data provided in this submission consist of summary tables only, therefore, we can draw no final conclusions from these data.

2. Chevron Chemical Co. must provide supporting scientific evidence for all data submitted, as follows:

i. Detailed protocols for monitoring studies must be submitted for RCB review. The source and number of analyzed samples must statistically represent the population tested.

ii. Field study samples must reflect the maximum registered dose and shortest PHI's. "Cooking" and processing studies should be described in detail, including any trimming, washing,... etc. of the commodity prior to cooking. Cooking time must also be stipulated.

iii. Information on storage of samples prior to analysis.

iv. Analysis of samples (full description of the analytical method and supporting quality assurance data, including control samples and recovery samples).

v. Calculation of analytical results (linear regression utilizing external standards, etc.).

v. Results of individual analyses, supported with representative chromatograms.

vi. Storage stability data.

RCB's Recommendation

The submitted data summaries provide insufficient information to permit a dietary exposure assessment. The registrant should provide supporting data for their data summaries as discussed in the text of this memo.

Other considerations

Note to PM: Once these data are adequately documented , RCB would incorporate all available data in an updated dietary exposure assessment for acephate/methamidophos, which we estimate will require 4-6 weeks to complete.

ATTACHMENTS:
1. Task 4: Exposure Profile, 3 pages.
2. RCB review (W. Hazel, memo of 5-4-85), 5 pages.
3. SIS review (K. Barbehenn, memo of 5-21-87), 3 pages.

cc:R.F.,S.F.,Circu,Acephate Reg. Std. file ,Reviewer,PMSD/ISB.
RDI:EZ:6/27/88:RDS:6/27/88
TS-796:FBS:fbs:557-1883:CM#2,RM814:6/27/88

Attachment #1

DYNAMAC
CORPORATION

ACEPHATE

Residue Chemistry

Task 4: Exposure Profile

Contract No. 68-01-5830

Final Report

January 28, 1982

Submitted to:
Environmental Protection Agency
Arlington, Virginia 22202

Submitted by:
Dynamac Corporation
Enviro Control Division
The Dynamac Building
11140 Rockville Pike
Rockville, MD 20852

ACEPHATE

Task 4

RESIDUE CHEMISTRY

Human Exposure - Dietary:

This Registration Standard for acephate is concerned with formulations containing the single active ingredient. Acephate is manufactured and sold by Chevron Chemical Company as Orthene 75% and 80% SC/L for use on food/feed crops; other formulations (G, P/T, SC/L, PrL) are used on ornamentals and forests. Acephate is an organophosphorus insecticide registered for use on beans, celery, cotton, lettuce, mints, peppers, soybeans, and tobacco. Approximately six to eight million pounds of active ingredient are applied annually in the United States; about two million pounds are exported annually. Major use sites are: ornamentals (32-34%), cotton (31-32%), tobacco (10%), lettuce (6-7%), beans (2-6%), and forests (2-5%). Other sites represent minor uses.

The theoretical contributions of acephate and its metabolite, methamidophos, to the human diet through the consumption of foods for which tolerances exist are presented in Table 1. The Acceptable Daily Intake (ADI) is 0.02 mg/kg/day and the Maximum Permissible Intake (MPI) is 1.2 mg/day based on a 60-kg human body weight. The Theoretical Maximum Residue Contribution (TMRC) is 0.4244 mg/day (35.37% of MPI) based on a 1.5-kg diet and utilizing the relevant tolerances and food factors for each food item. The food items contributing the highest residues to the diet are lettuce, beans, celery, and milk and dairy products (Table 1).

Table 1. Acephate tolerances for various food items and their contribution to the human diet.

Food item	Tolerance[a] (ppm)	Food factor	TMRC (mg/day)[b]	Percent of total TMRC
Beans	3.0[c]	2.04	0.09180	21.6
Celery	10.0[c]	0.29	0.04292	10.1
Cottonseed (oil)	2.0	0.15	0.00450	1.1
Eggs	0.1	2.77	0.00416	1.0
Lettuce	10.0[c]	1.31	0.19622	44.8
Meat (including poultry)	0.1	13.85	0.02077	4.9
Milk and dairy products	0.1	28.62	0.04292	10.1
Peppers	4.0[c]	0.12	0.00736	1.7
Soybeans (oil)	1.0	0.92	0.01377	3.2
			Total 0.42442	

[a]According to 40 CFR 180.108.

[b]TMRC based on a diet of 1.5 kg/day.

[c]No more than 1 ppm may be methamidophos.

Attachment #2 Reg. Stand Fib

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

14 MAY 1985

EXPEDITE

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Feasibility of reducing the dietary exposure to acephate and its metabolite methamidophos.

FROM: William J. Hazel, Ph.D., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

William J. Hazel

THRU: Charles L. Trichilo, Ph.D., Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

TO: William H. Miller, PM #16
Insecticide - Rodenticide Branch
Registration Division (TS-767)

A request has been forwarded (4/17/85) from Anne Barton for an expedited review of the RCB data base conducive to a more realistic estimation of human dietary exposure to acephate residues. Human dietary exposure to acephate residues based on the TMRC was determined to represent an unacceptable risk in light of the potential oncogenicity of acephate. Procedures such as washing, trimming, cooking, storing, or processing of raw agricultural commodities (RAC) may result in reductions in dietary exposure to acephate residues. This may, in turn, reduce the risk to an acceptable level upon subjection to risk-benefit analysis.

On 4/12/85, RCB received from Edwin Budd (TOX) acephate dietary exposure data generated by the Tolerance Assessment System (TAS). The following populations were chosen because they are representative and/or their theoretical maximum dietary exposure to acephate residues was greater than the ADI: (i) U.S. population - 48 states (78% of ADI); (ii) children 1-6 years old (190% of ADI); and (iii) non-nursing infants <1 year old (212% of ADI). The foods contributing >1% of the ADI for one or more of these populations are: celery, lettuce, green succulent beans, dry beans (navy and pinto), soybean defatted flour and oil, citrus juice and pulp, fresh apples and juice, and milk [nonfat solids, fat solids, and sugar (lactose)]. The present review will concern only these foods because these represent the principal sources of dietary exposure to acephate. Note that apple products contribute 6.4-64% of the ADI but that a temporary tolerance has been established for acephate residues in or on apples (PP# 3G2790). Also note that citrus products account for 47-129% of the ADI but that a temporary tolerance is pending (PP# 3G2807) for citrus.

The adequacy of the available data to estimate dietary exposure to acephate residues was determined for those commodities having established tolerances, as discussed below. Deficiencies are noted where appropriate.

It should be noted that limited cooking (boiling) and canning data are available but that the results are inconclusive. The canning data are discussed below under "Beans, succulent". One cooking study, involving cabbage, broccoli, and tomatoes (commodities not listed above) showed no loss of residues of acephate or its metabolite methamidophos after boiling for 0.5 hour but did not distinguish between residues in the cooking water and those in the food item. A second cooking study indicated that 60-80% of the residues in Brussels sprouts were transferred to the cooking water. This suggests that cooking and canning are likely methods of reducing dietary exposure. However, the percentage of residues lost upon cooking or canning is expected to depend upon the commodity in question and, therefore, studies should be conducted on each crop individually. Also, it should be noted that cooking fluids may be consumed (such as celery in soup or dry bean canning liquids).

Beans, succulent: Available canning data are quite variable for residues of both acephate and methamidophos and, in addition, sampling was inadequate. Canning does, however, appear to be a potential route of dietary exposure reduction. Residues of acephate and methamidophos, respectively, in two canned bean samples (two relicates of each) were 0.19-0.65 ppm and 0.24-0.44 ppm. These represent 12-58% and 34-65% of the respective residues determined in/on the RAC. Residues of acephate and methamidophos in two samples (two replicates each) of canning water were 0.18-0.73 ppm and 0.25-0.50 ppm, respectively. No cooking (boiling) data are available on beans. Available FDA monitoring data (46 RAC samples) reveal no above tolerance residues. Residue data are insufficient to allow an increase in the preharvest interval (PHI), if this is considered an option. The following data are needed to estimate actual dietary exposure in succulent beans:

° Cooking (boiling) of succulent green beans according to common consumer practices. Beans must bear field-weathered, detectable residues of acephate and methamidophos. Beans must be analyzed both before and after cooking. Cooking water should also be analyzed.

° Commercial processing (canning) of field-treated, succulent green beans bearing detectable residues of acephate and methamidophos. Beans must be analyzed both before and after canning. Canning water should also be analyzed.

Beans, dried: No canning or cooking data are available. Data are insufficient to support an increase in the PHI, if desired. The following data are needed to estimate the actual dietary exposure to residues in dry beans:

° Pinto and/or navy beans must be field-treated with the 75% soluble concentrate/solid formulation (SC/S) six times at 1 lb ai/A. Beans are to be allowed to dry normally, and then both boiled and canned, in separate tests, according to typical home or commercial preparation procedures. Cooking fluid and beans must be analyzed both before and after boiling and canning for residues of acephate and its metabolite methamidophos.

Celery: The available data at the established 21-day PHI are adequate to allow an estimation of dietary exposure due to the consumption of raw treated celery, trimmed as per label instructions. At the 21-day PHI, residues of acephate and methamidophos in or on trimmed celery following 5-10 treatments at the maximum rate were 0.31-3.38 ppm and nondetectable (ND, <0.01 ppm) -0.24 ppm, respectively. These data represent seven tests conducted in CA, FL, and NJ.

Data are available to increase the PHI up to 35 days, thereby decreasing residues if desired. Washing and cooking data are not available. Celery is generally washed after harvest and also is frequently hydrocooled; the effect of a third wash on acephate residues may not be significant and, as a consequence, data on this topic are optional. Cooking is expected to reduce residues further. However, since celery contributes $\leq$ 3.2% of the ADI to the diet and since most celery is consumed fresh (raw), we will not recommend that celery cooking data be submitted.

Monitoring data collected by FDA (10/1/82-1/10/85) involving 56 celery samples indicate no above tolerance residues of acephate or methamidophos; residues were detected at 0.01-1.7 ppm and 0.01-0.76 ppm, respectively.

Lettuce, crisphead: The available residue data, supported by FDA monitoring data, are adequate to determine the actual dietary exposure to acephate residues from crisphead lettuce consumption. Since crisphead lettuce is generally trimmed to bear 3-5 wrapper leaves, we can use the data available for trimmed heads (number of wrappers unspecified) and for heads plus six wrapper leaves 14 or 21 days, respectively, after the last of 4-9 applications of the 75% SC/S at 1 lb ai/A (1x). Residues of acephate and methamidophos in or on lettuce were 0.19-4.42 ppm and 0.02-0.49 ppm, respectively.

Residues of acephate and methamidophos were detected at 0.01-2.00 ppm and 0.01-2.20 ppm, respectively, in or on 153 lettuce samples monitored by FDA from 10/1/82-1/10/85. Methamidophos residues were generally $\leq$0.35 ppm. Note that methamidophos residues in or on some samples may result from treatment with methamidophos formulations. No additional data are needed at this time.

Soybean oil: The available processing data are not adequate to estimate the dietary exposure due to consumption of soybean oil.

Acephate and methamidophos residues were found at <0.02(ND)-0.03 ppm and <0.01 ppm (ND), respectively, in three crude soybean oil samples processed from soybeans 14 or 15 days after the last of three applications at the maximum rate (1 lb ai/A). A 14-day PHI is in effect. Acephate residues in crude oil may be present at $\leq$33% of the concentration in or on soybean seed. Cottonseed data indicate that further reductions in residues would occur upon refining the crude oil but data are insufficient to make a reliable estimation. A worst-case estimate (assuming that refined oil residues are 33% of those in seed) will be used unless the registrant wishes to submit the following:

° A determination of residues of acephate and methamidophos in crude oil and refined oil.

Soybean, defatted flour: Defatted soybean flour, used as a component of infant formulae, may contribute 3.8% of the ADI to non-nursing infants (<1 year old). The available data for soybean mill feed (presumed to contain the same level of residues as soybean meal) in the absence of data on defatted flour reveal acephate residues of <0.02 ppm (ND) to 0.34 ppm and methamidophos residues of <0.01 ppm (ND) to 0.07 ppm in three samples processed from beans 14 or 15 days after the last of three treatments at 1 lb ai/A (1x). Beans contained combined residues $\leq$ 0.21 ppm. Defatted flour is similar to soybean meal but has not been toasted and is more finely ground. A four-fold residue concentration generally occurs upon processing soybeans to soybean meal (and, presumably, defatted flour), as reflected by the 1 ppm vs. 4 ppm tolerances in or on seed vs. meal, respectively. No additional data are needed concerning defatted soybean flour. However, the registrant should know that we will utilize the worst-case estimate (four-fold concentration from soybeans to defatted flour) unless the following study is submitted:

° A determination of the degree of concentration (or reduction) of acephate and methamidophos upon processing soybeans (containing field-weathered residues) to defatted flour.

Milk: Dairy products contribute 4.2-26.1% of the ADI, depending on the population under consideration. The TAS recognizes three milk fractions: non-fat milk solids, milkfat solids, and milk sugar (lactose). Whole milk from cattle fed acephate and methamidophos at a combined level of 3.6 ppm (1x the maximum expected dietary intake) contained acephate at $\leq$0.05 ppm and methamidophos at <0.005 ppm (ND). However, no data are available concerning the fate of residues upon pasteurization or processing into the fractions noted above. The following data would be needed for an actual exposure assessment:

° A dairy cattle feeding study must be conducted in which cattle are fed acephate and methamidophos at an approximately 5:1 ratio in the diet. The feeding level should be high enough to result in detectable residues of both acephate and methamidophos in milk. Exaggerated rates would be advantageous. Residues of acephate and methamidophos must be determined in whole raw milk (containing detectable residues of each compound), pasteurized milk, and in non-fat milk solids, milkfat solids, and possibly milk sugar (lactose).

No FDA monitoring data are available on acephate or methamidophos residues in milk.

Tolerances have not been established for acephate residues in or on apples or citrus but, as noted above, a temporary tolerance has been established or is pending, respectively, for each of these commodities which contribute greatly to the dietary exposure. It would be advisable for the registrant to submit relevant dietary exposure data on these commodities as a part of any petition proposing a tolerance for acephate residues in or on apples or citrus if, indeed, any new food uses are allowed in the future. Relevant data may involve the whole fruit (washed and unwashed), the peeled fruit, the juice, cooked fruit (including applesauce and baked apple products), and canned fruit (cooking and canning fluids should also be analyzed).

cc: S.F., R.F., R.S.File, Reviewer, TOX, PMSD(ISB), Anne Barton
TS-769:RCB:WH:bj:RM-810:CM#2: X557-7484: 5/2/85

Attachment #3

E. Hazel
R.C.B

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

MAY 21 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Acephate - Status of the ADI and the TMRC

TO: William H. Miller, PM 16
Insecticide-Rodenticide Branch
Registration Division (TS-767C)

THRU: Amy S. Rispin, Director
Science Integration Staff
Hazard Evaluation Division (TS-769C)

Amy Sue Rispin

As indicated in Reto Engler's memo of February 10, 1987, there is some uncertainty over the most appropriate ADI for acephate and a clearer resolution of this issue should be made by conducting a sub-chronic study for brain ChE inhibition in the rat. For now it appears that a PADI of 0.0025 mg/kg/day is adequate, pending resolution of the issue. Since the present TMRC for published tolerances is about 250% of this PADI, I have made a preliminary assessment of maximum likely dietary exposure.

Six commodities produce about 90% (.41/.46 mg/day) of the TMRC (Table 1). Of these, tolerances for lettuce (crisphead), celery and beans are set at about 2 or 3 times the maximum levels observed in field trials. FDA surveillance records indicate that maximum residues observed for celery and lettuce were somewhat less than that in the field trials (Hazel memo, 5/14/85). The field trial values, therefore, provide a reasonable worst case estimate for dietary exposure. Residue data for soybean oil and for animal products are less adequate but the observed values in Table 1 provide a reasonable estimate.

Estimates of domestic usage of acephate for 1980 (PQUA, Scheid, October 1980) indicate that most of the head lettuce and celery is treated (Table 1). For the purpose of estimating subchronic exposure, it should be assumed that all of these RAC's are likely to have been treated. On the other hand, relatively small amounts of the beans and soybeans are exposed to acephate and market-place dilution should reduce sub-chronic exposure accordingly. Relatively small amounts of animal feed consist of acephate treated material and residues

should be transient with little potential for sub-chronic exposure. Dietary exposure, therefore, was adjusted by multiplying the maximum residues observed by the percentage of the crops treated.

On the average, dietary exposure to acephate is not likely to exceed 0.104 mg/day (Table 1). For a 60 kg person, this is 69% of the PADI. By far the greatest contribution to dietary residues is lettuce and it is reasonable to expect that many individuals will consume substantially more lettuce than the average. This should be counterbalanced by the fact that not all "lettuce" is crisphead and that the average residues expected should be significantly less than the maximum observed.

The available information suggests that actual dietary exposure for salad eaters is somewhat less than the current PADI. A more refined estimate would require an analysis of the statistical distribution of residues on lettuce and celery. Since these RAC's account for almost all of the expected subchronic exposure to acephate, processing studies other than those previously requested should not be necessary.

Kyle Barbehenn, Biologist
Science Integration Staff
Hazard Evaluation Division (TS-769C)

cc: Anne Barton
Reto Engler
Bill Hazel

TABLE 1.

MAXIMUM LIKELY MEAN DIETARY EXPOSURE FOR ACEPHATE

	Theoretical Maximum		Maximum Likely		
Commodity	Tolerance (ppm)	mg/day	Max. Obs. (ppm)	% Crop Treated	mg/day
Lettuce	10	.20	4.4	100	0.088
Celery	10	.044	3.4	100	0.015
Beans	3	.092	1.2	<1	4×10^{-4}
Soybean Oil	1	.014	0.03	1-2	1×10^{-5}
Meat	0.1	.021	NA	<1	2×10^{-5}
Milk	0.1	.043	$\leq$0.05	<1	2×10^{-4}
SUBTOTAL		.41			0.104