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To: Jay Ellenberger/Ed Allen
Product Manager (12)
Registration Division (TS-767)

From: Carolyn K. Offutt [signature]
Chief, Modeling and Guidelines Section
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Attached please find the environmental fate review of:

Reg./File No.: 352 - 366

Chemical: Methomyl

Type Product: Insecticide

Product name: Lannate

Company name: Du Pont

Submission Purposes: Data submission in response to a Registration Standard requirement for reentry/fieldworker protection

ZBB Code: ______

Action Code 606

Data In: 10/14/83

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Deferrals To:

___ Ecological Effects Branch

___ Residue Chemistry Branch

___ Toxicology Branch

1/31/85

REVIEW OF METHOMYL REENTRY DATA SUBMITTED BY DUPONT IN RESPONSE TO A REGISTRATION STANDARD

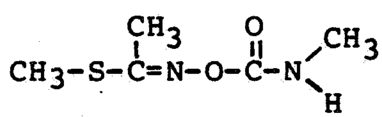
1.0 INTRODUCTION

EPA requires in 40 CFR § 158.140 that registrants must submit data for evaluation of a pesticide's hazard to fieldworkers if the pesticide meets certain criteria. Among the criteria are: 1) acute toxicity of the pesticide is such that the pesticide would be classified in Toxicity Category I, or the pesticide has been implicated in fieldworker poisonings; and 2) the pesticide is used on crops in which agricultural practice requires human tasks that involve substantial contact with residues of the pesticide. Methomyl meets both the toxicity and exposure criteria of 40 CFR § 158.140; and data were, therefore, required under a Registration Standard for Methomyl. In response to that Standard, DuPont has submitted data. This is a review of that data.

Methomyl has been implicated in fieldworker poisoning episodes in California. In response to these complaints, the California Department of Food and Agriculture [CDFA] has established reentry intervals for methomyl ranging from 24 hours to 4 days depending on the crops.

2.0 PESTICIDE STRUCTURE/NOMENCLATURE

Methomyl: Acetimidothioc acid, methyl-, N-(methylcarbamoyl) ester



Other names are: Lannate; Nudrin; DuPont 1179; S-methyl N-[(methylcarbamoyl)oxy]thioacetimidate; and 3-thiabutan-2-one, O-(methylcarbamoyl)oxime.

Molecular Formula: $C_5H_{10}N_2O_2S$ Molecular Weight: 162.2 Daltons

3.0 DISCUSSION

Under the Registration Standard (Task 2. pp. 19-20) and Subdivision K of the Guidelines, the registrant is allowed three major options for the estimation of reentry intervals. Du Pont has chosen the second option by submitting dislodgeable-residue-data dissipation-curves for methomyl applied to a number of crops and even varieties of some crops. It appears that all of this data was previously submitted to the CDFA and was gathered in that environment. Since it is recognized that California's meteorological conditions are generally the least conducive to dissipation of dislodgeable residues in the United States, data gathered in California are acceptable for establishment of reentry intervals for other environmental conditions in the United States.

Their approach to the calculation of reentry intervals from the dislodgeable residue data is to use Dr. J. Knaak's [CDFA] method and his calculation of a reentry level for methomyl. Knaak's method for the calculation of a reentry interval has been shown to yield essentially the same reentry intervals as the Agency model/method detailed in Subdivision K of the Pesticide Assessment guidelines. Therefore, Du Pont's approach here is valid.

Knaak's method involves calculation of a reentry level from a known allowable reentry level for a standard pesticide in conjunction with the dermal-dose erythrocyte-acetylcholinesterase response data obtained with rats by Knaak's method. [It should be noted here that Knaak's data indicates significant acetylcholinesterase reduction from dermal doses of methomyl even though Du Pont maintains that there is no dermal hazard for the pesticide because of a low acute dermal toxicity (>5000 mg/kg).] Knaak has determined experimentally that an allowable reentry level for methomyl on citrus foliage is 1.55 ug/cm^2. This level is based on the inhibitory effect of dermal doses of methomyl on acetylcholinesterase. It is not relevant if animals, and therefore people, are more sensitive to methomyl through some other mode of toxic effect.

The Registration Standard required that the Registrant submit data and propose reentry intervals for several crops [Task 2. p. 20] that are listed in the first column of Table 1 of this DER. The Registrant is submitting dislodgeable residue data for the crops listed in the second column of Table 1. The Registrant is not submitting data for all of the crops listed in the registration standard. However, this approach is acceptable because residue data from the most hazardous crops are included, and the data can be used for other crops on a worst case basis.

Data are required for those crops which have agricultural practices such as harvesting, thinning, etc. that involve substantial human contact with foliage or soil subsequent to methomyl application. Requirement of data does not necessarily mean that reentry intervals will be required for the pesticide for all or any of its registrations; but if the data do show an unreasonable risk, reentry protection statement/interval(s) will be required for placement on the pesticide's labeling.

Except for the summaries, this submission consists of 12 Exhibits. Exhibits 1, 2, 7, 8, 9, and 11 consist of published papers and CDFA reports or reports submitted to CDFA.

Exhibit 3 contains a summary of methomyl dislodgeable-residue recoveries from recovery studies conducted at the Du Pont and Stoner (contractor) laboratories. Exhibit 3 also contains summaries of the dislodgeable residue dissipation data.

Exhibit 4 contains dislodgeable residue data and dissipation curves for methomyl applied to grape, orange, peach, and nectarine foliage. The primary thrust of this exhibit was to petition for the CDFA reentry interval of 4 days to be reduced to 24 hours. Exhibits 5 and 6 consist of methomyl dislodgeable residue studies on ornamentals and corn, bean, and cabbage plants, respectively.

They also submit fieldworker health data to support their contention that methomyl is not a significant hazard to fieldworkers. Those data are contained in: 1) Exhibit 9 which is a sort of epidemiology study of people working in fields treated with methomyl; 2) Exhibit 12 which is a copy of the 1981 PIMS report; 3) Exhibit 10 which is a report of cholinesterase activity levels in workers sampling foliage for dislodgeable residue determination; and 4) Exhibit 11 which contains a melange of toxicity and metabolism studies, several graphs of methomyl dissipation, a published paper on dissipation of insecticides from cotton, a 1975 reentry paper by Spear et al., calculations for estimation of methomyl inhalation exposure, and a report that industrial exposure to methomyl has not caused symptoms in their workers.

(1) Evaluation of the foliar residue data

Except for the published papers included in the exhibits the experimental procedures for methomyl residues collection, extraction, and quantitation contained in this submission are cursory. There is a short, but valid, estimate of surface residues that can be easily removed by their procedure and a statement that "Methomyl is soluble in water to the extent of 5.8 grams per 100 grams of water." That implies that the extraction was done with water without detergents. This does not coincide with the methodology suggested in Subdivision K but appears to be adequate. The recovery data for rose, chrysanthemum, and carnation foliage reported in their Exhibit 5 indicates that it is minimally adequate. They have submitted a table (Table I of Exhibit 3) of recovery data to support their submitted dissipation data.

The submission also contains data as "dislodgeable residue data". The use of the term "Dislodgeable Residues" is usually taken to mean employment of the procedure of that name developed by Drs. F. A. Gunther and Y. Iwata, but it is questionable that that was the procedure that was used to gather the data. They do not cite the appropriate methodology papers, and they did not originally use leaf punches for foliar sampling as is done in the Dislodgeable Residue procedure (although they later used leaf punches to estimate leaf weight to surface ratios). Much if not all of the submitted data were gathered before 3/31/1976 which could be before the Dislodgeable Residue method came to their attention.

Much of the dislodgeable residue data that Du Pont submits was gathered on whole leaves rather than on a known foliar surface area. That is, their original data was expressed in parts per million of leaf weight. [N.B.: In this case, the reports in ppm do not mean that the penetrated residues were quantified as well as dislodgeable residues.]

(2) Ratios of Foliar Weight to Surface Area

For implementation of either the CDFA's or the EPA's methods for calculation of reentry intervals, the dislodgeable residue data must be expressed in weight of residue per cm^2 of leaf surface. For that reason, the registrant had to convert the whole-leaf residue values in parts per million to leaf-surface values in ug/cm^2. This has been done in the data submitted, but the reporting of how the conversion factors were determined and calculated is cursory.

The data that they have submitted for estimation of foliar weights per unit surface-area are important here because those ratios are used to convert their whole-leaf residue data from parts per million to weights per unit area, i.e. ug/cm^2. The residue data in ug/cm^2 are then used to estimate exposure levels. Thus, the weight to area ratios affect the estimated worker-exposure rates and the estimated reentry intervals.

In Table XXI of their Exhibit 3, they report data and the calculations for estimation of the surface to weight ratios for nine types of foliage. Their calculations are based on two sides of the leaves. [Some investigators have based their work on one side of the leaf, and this must be recognized when surrogate exposure data are used.] They report replicates of the total weight of 50 leaf-disk samples. Generally they cut 2.54 cm (1 inch) disks, but in the case of carnations they cut 0.317 cm^2 disks. They have 3 leaf-disk weight-replicates for grape, rose, carnation, and pinto-bean foliage; 4 replicates for nectarine, orange, cabbage, and cotton foliage, but only one replicate for chrysanthemum foliage.

The table below presents a summary of their ratios and similar ratios for two types of grass from other studies for comparison.

REPORTED LEAF WEIGHT TO AREA RATIOS

Type of Plant Foliage	Weight/Area Ratio (Two Sides: mg/cm^2)
Grapes	10.92
Nectarines	12.70
Oranges	13.12
Roses	8.68
Carnations	10.41
Chrysanthemums	22.50
Pinto Beans	6.97
Cabbage	29.95
Cotton	8.60
Grass, California	6.83
Grass, North Carolina	10.09

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(3) Calculation of an allowable exposure level

The following calculation is according to methodology presented in Subdivision K of the Pesticide Assessment Guidelines. It is based on: a) Dermal Penetration (DP) factor of 1 since appropriate dermal penetration data are not available; b) a No Observed Effect Level (NOEL) of 2.5 mg/kg/day from a 2-year chronic feeding study in which prostate and kidney effects were observed at higher doses; and c) on a 100 Safety Factor which is used for chronic effects of this type. The calculation is also based on an 8-hour work day and a 70 kg body weight for a fieldworker.

$$AEL = \frac{(NOEL)(BODY\ WEIGHT)}{(SF)(DP)(8\ hr/d)} = \frac{(2.5\ mg/kg/d)(70\ kg)}{(100)(1)(8\ hr/d)}$$

$$= 220\ ug/hr$$

(4) Estimation of the reentry level

* The corresponding reentry level is 50 ng/cm^2 [from Popendorf's correlation]. This is 30 times less than the ChE reentry level determined by Knaak (1.55 ug/cm^2).

(5) Estimation of reentry intervals for methomyl

The dislodgeable residue and application rate data contained in this submission are summarized in Table 2. The foliar residue data reported for corn were not converted from ppm to weight per area values in the submission nor is there a weight to area ratio reported. For that reason, it is not possible convert the data to a useable form, and the corn data is not considered here. The foliar residue data in this submission show the high variability commonly reported in such studies. For that reason, I have averaged data points to increase reliability wherever possible. Wherever the dislodgeable residue level was not reported for a period, I have taken the previous date's datum as a surrogate in order to calculate an average (mean) for that period.

REENTRY INTERVAL FOR ORANGE/CITRUS

The means of dislodgeable residue data for orange foliage at 33 ng/cm^2 indicate that a 3-day reentry interval is appropriate.

REENTRY INTERVAL FOR GRAPES

The reported dislodgeable residue levels for grape foliage are higher than for orange foliage even though the pesticide usage rates are the same. The data indicate that methomyl tends to be more persistent on grape foliage under conditions of the test. Even though the data is highly variable, the dissipation rate is clearly lower for grape foliage than for orange foliage. The data reported are based on application of 1.8 lbs of active ingredient per acre (a.i.a.) even though they state that the maximum usage is now 0.9 lbs a.i.a. The use of data from the 1.8 lb a.i.a.

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applications can be used for this review because residues from application of 0.9 lb a.i.a. would be less and the exposure would be less.

There are graphs of grape foliar residue dissipation presented in Exhibit 4 that are not presented as data in Exhibit 3. In order to track the data in Exhibit 4 with that in Exhibit 3, note that data in their Table II (1st and 3rd sprays) correspond to "exhibits 3A and 3B, but "4th spray" does not correspond to "exhibit 3C". Their Table III (1st and 3rd spray) correspond to "exhibit 5A" and "exhibit 5B" in Exhibit 4; but data in their Table III (5th spray) do not represent "exhibit 5C". Their Table IV (1st and 3rd spray) correspond to "exhibit 4A" and "exhibit 4B" in Exhibit 4; but data in their Table III (5th spray) do not represent their "exhibit 4C". Their Table V (1st and 3rd spray) correspond to "exhibit 6A" and "exhibit 6B" in Exhibit 4; but data in their Table V (5th spray) do not represent their "exhibit 6C". The differences in residue levels coincide with a change of analytical laboratory. These differences should be resolved.

The means of dislodgeable residue data for grape foliage are not less than 50 ng/cm^2 until the 7th day after application (when they are 16 ng/cm^2). This indicates that a 7-day reentry interval is appropriate. Interpolation of the data is not possible until there is a resolution of the discrepancy between the data and graphs.

REENTRY INTERVAL FOR PEACHES

The means of dislodgeable residue data for peach foliage are not less than 50 ng/cm^2 until the 4th day after application (when they are 38 ng/cm^2). This indicates that a 4-day reentry interval is appropriate.

REENTRY INTERVAL FOR NECTARINES

The means of dislodgeable residue data for nectarine foliage are not less than 50 ng/cm^2 until the 3rd day after application (when they are 19 ng/cm^2). This indicates that a 3-day reentry interval is appropriate.

REENTRY INTERVAL FOR COTTON

The dislodgeable residue data for cotton foliage are not less than 50 ng/cm^2 through the 3rd day after application when they are 55 ng/cm^2. A 3-day reentry interval appears to be appropriate.

REENTRY INTERVAL FOR MINT

Data have been submitted for residues on mint foliage after application of 0.9 and of 1.8 lb a.i.a. In neither case do the residues dissipate to the 50 ng/cm^2 level at any of the sample dates. Thus it is not possible to establish a reentry interval for mint with the submitted data.

REENTRY INTERVAL FOR ROSES

Dissipation data have been submitted for indoor and outdoor use of methomyl on roses, chrysanthemums, and carnations. The data were taken at short intervals with the last samples taken 24 hours after application.

The means of dislodgeable residue data for rose foliage outdoors are less than 50 ng/cm^2 after 24 hours application (when they are 20 ng/cm^2). This indicates that a 1-day reentry interval is appropriate for roses when grown out of doors. However, the data indicate that methomyl dissipation in the greenhouse is slower than out of doors. When the crop is grown in a greenhouse, the means of dislodgeable residue data for rose foliage is not less than 50 ng/cm^2 after 24 hours application (when they are 286 ng/cm^2). This indicates that a 1-day reentry interval is not adequate for that situation. No data at later sampling dates were reported so it is not possible to establish a rose-greenhouse reentry interval for methomyl with the available data.

REENTRY INTERVAL FOR CHRYSANTHEMUMS

Again the methomyl dissipation rate in the greenhouse is slower than out of doors, but in no case do the foliar residues dissipate to or less than the reentry level at 24 hours after application. Thus, it is not possible to set reentry intervals with the available data.

REENTRY INTERVAL FOR CARNATIONS

In both indoors and outdoors data, the foliar residue levels have dissipated to less than 50 ng/cm^2 at 24 hours after application. Therefore, a one day reentry interval is appropriate for work in carnations either outdoors or in a greenhouse.

REENTRY INTERVAL FOR BEANS AND CABBAGES

Foliar residue levels for both beans (at 31 ng/cm^2) and cabbage (at 13 ng/cm^2) have dissipated to less than the reentry level within 6 hours after application. Therefore, a 24 hour reentry interval is appropriate.

4.0 CONCLUSIONS

The submitted data in concert with toxicological information indicate the following reentry intervals are appropriate: one day for beans, cabbages, roses grown outdoors, and carnations whether grown outdoors or in a greenhouse; three days for cotton, nectarines, and oranges/citrus; four days for peaches; and 7 days for grapes. Although there is limited dissipation data for several other crops, it is not possible to determine an appropriate reentry interval for them either because the foliar sampling was not conducted long enough [e.g. mint, roses in greenhouses, and chrysanthemums in greenhouses or outdoors] or because the data could not be converted to weight-per-area values for lack of a conversion factor [e.g. corn, celery, lettuce, spinach].

Because of similarity in crops and the work tasks performed in those crops, I believe that a 3 day reentry interval would be adequate for work in apple orchards and that a 1 day reentry interval would be adequate for alfalfa, asparagus, brocoli, brussel sprouts, carrots, cauliflower, celery, collards, cucumbers, lettuce, melons, onions, peanuts, peas, peppers, potatoes, sorhgum, soybeans, summer squash, spinach, sugar beets, tobacco, and tomatoes.

5.0 RECOMMENDATIONS.

The Registrant should be required to submit further data for mint, roses in greenhouses, and chrysanthemums in greenhouses or outdoors and to submit weight/area conversion factors for corn foliage (for reentry protection of detasselers). The Registrant should also be required to place the above reentry intervals on his labels.

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TABLE 1

LIST OF FOLIAR DISLODGEABLE RESIDUE DATA BY PLANT/CROP

DATA REQUIRED BY THE REGISTRATION STANDARD	DATA CONTAINED IN DU PONT SUBMISSION
1. citrus	orange
2. grapes	grapes
3. peaches	peaches
4. nectarines	nectarines
5. alfalfa	
6. apples	
7. asparagus	
8. beans	beans
9. brocoli	
10. brussel sprouts	
11. cabbage	cabbage
12. carrots	
13. cauliflower	
14. celery	
15. collards	
16. corn	corn
17. cotton	cotton
18. cucumbers	
19. lettuce	
20. melons	
21. mint	mint
22. onions	
23. peanuts	
24. peas	
25. peppers	
26. potatoes	
27. sorhgum	
28. soybeans	
29. summer squash	
30. spinach	
31. sugar beets	
32. tobacco	
33. tomatoes	
34. trees, forest	
35. ornamentals	ornamentals rose chrysanthemum carnation

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TABLE 2

SUMMARY OF DISLODGEABLE RESIDUE DATA SUBMITTED

Type of foliage	Dislodgeable Residue Data, ng/cm^2 at an Interval After Application						Pesticide Treatment Level
	4 hr	1 d	2 d	3 d	4 d	7 d	
ORANGE							
Navel	5	<3	<3	<3			1.8 lb a.i.a.
	315	84	123	76			"
	236	92	42	13			"
Valencia	10	<3	3	<3			"
	102	81	197	87			"
	171	126	31	16			"
averages	140	65	67	33			
GRAPE							
Thompson IIa	15	142	70	39	2	< 2	1.8 lb a.i.a.
" IIb	1267	415	70	153	87	15	"
" IIc	633	197	44	22	39	31	"
IIIa	131	120	65	28	28#	13*	"
IIIb	458	79	100	46	92	44*	"
IIIc	74	100	26	4	4#	24*	"
Palomino IVa	764	186	131	142	33	13	"
IVb	786	306	218	218	349	20	"
IVc	306	142	41	9	4	6	"
Cabernet Va	349	197	120	85	85#	2*	"
Vb	480	284	262	131	240	20	"
Vc	197	131	33	11	11#	4*	"
averages	455	192	98	74	82	16	
PEACH	229	94	99	81	28		1.8 lb a.i.a.
	241	178	96	-	-		"
	51	178	107	53	38		"
averages	174	150	101	67	38		
NECTARINE	140	70	58	15			1.8 lb a.i.a.
	203	86	46	23			"
averages	172	78	52	19			
COTTON	5930	1220	115	55			0.5 lb a.i.a.
MINT	1520	707	333				0.9 lb a.i.a.
	2297	1233	627				1.8 lb a.i.a.

= datum taken from previous date's to replace missing datum

* = residues at 6 days

TABLE 2 [continued]

SUMMARY OF DISLODGEABLE RESIDUE DATA SUBMITTED

Type of foliage	Dislodgeable Residue Data, ng/cm^2 at an Interval After Application					Pesticide Treatment Level
	1 hr	2 hr	4 hr	8 hr	24 hr	
ORNAMENTAL						
rose;						
outdoors	564	460	451	234	18	0.45 lb a.i.a
	712	651	556	503	21	"
averages	638	556	504	369	20	
greenhouse	755	738	955	825	286	0.45 lb a.i.a
	781	1160	868	668	373	"
averages	768	949	912	747	330	
chrysanthemum						
outdoors	1845	2003	1463	1125	27	0.45 lb a.i.a
	1240	1890	1485	990	248	
averages	1543	1947	1474	1058	138	
greenhouse	755	738	955	825	286	0.45 lb a.i.a
	781	1160	868	668	373	"
averages	768	949	912	747	330	
carnation						
outdoors	489	271	208	148	17	0.45 lb a.i.a
	354	343	115	104	19	
averages						
greenhouse	115	146	146	72	11	0.45 lb a.i.a
	115	167	135	82	4	"
averages	115	157	141	77	8	
	0 hr	2 hr	6 hr	12 hr	24 hr	
BEAN	153	118	31	15	11	0.5 lb a.i.a.
CABBAGE	51	45	13	15	7	0.5 lb a.i.a.

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