July 17, 79

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

CASWELL#378A

DATE: July 17, 1979

SUBJECT: Section 18 - Specific Emergency Exemption for the Use of Monitor (O,S-Dimethyl Phosphoroamidothioate) on Celery to Control Leafminers. Shaughnessy#101201 Caswell #378A

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TO: Hoyt Jamerson
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THRU: Dr. Adrian Gross, Chief
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Discussion

A specific emergency exemption for the use of Monitor on celery to control leafminers is requested by the state of Florida.

The actual product proposed for usage is Monitor 4, 40% of which is the active ingredient.

The proposed rate of application is 1-2 pints of Monitor 4/acre. Applications are to be made at 7-day intervals with a maximum of 5 applications onto approximately 6,500 acres during the growing season of June, 1979 to June, 1980. The interval between treatment and harvest will be 21 days.

The inert ingredients are cleared under CFR 180.1001(c).

The requested residue tolerance is 2 ppm in or on celery. In a previous memo by D. Ritter, TOX, on PP#6E1794 (2/24/77), this tolerance was disapproved on the basis that the theoretical ADI was exceeded and oncogenic potential was not fully defined. However, in a subsequent memo by Ritter on PP#6E1794 (8/24/77), it was concluded that this tolerance could be approved according to reasons supplanting objections in the 2/24/77 memo and that this usage of Monitor would not pose an undue hazard to human health. The present Section 18 exemption request previously has been granted, based on the recommendation in the 8/24/77 Ritter memo, per additional memos by Ritter (1/12/78 and 9/6/78).

Tolerances previously established for Monitor under CFR 180.315 include 1 ppm in or on broccoli, brussels sprouts, cabbage, cauliflower, cucumbers, eggplant, lettuce, peppers and tomatoes; 0.5 ppm in or on melons; 0.1 ppm in or on cottonseed and potatoes. Furthermore, tolerances granted for acephate (Orthene) under CFR 180.108 included the stipulation that no more than 1 ppm of the residue in each of the following vegetables can be Monitor, a metabolite of acephate: celery, head lettuce, bell peppers, and beans.

EPA FORM 1320-6 (REV. 3-76)

Previously, the proposed section 18 has been approved by CHM, contingent on provisions described in a memo by R.D. Perfetti, 1/9/78. Included in the Perfetti memo is the requirement that acephate is not to be used with Monitor in the same season.

Toxicity data previously submitted in support of tolerance petitions for Monitor include the following:

Acute Oral LD50 (rat)[a]	95% Technical	15.6 mg/kg (M) 13.0 mg/kg (F)
	75% Technical	21.0 mg/kg (M) 18.9 mg/kg (F)
90-day Feeding (rat)[a]	75% Technical	NEL (erythrocyte cholinesterase) = 0.3 - 1.0 ppm
90-day Feeding (dog)[a]	75% Technical	NEL not determined due to variability in cholinesterase assays
90-day Feeding (dog)[b]	Technical	NEL (cholinesterase) = 3 ppm.
90-day Feeding (dog)[b]	Technical	NEL (cholinesterase) = 1.5 ppm.
90-day Feeding (rat)[b]	Technical	NEL (erythrocyte cholinesterase) = 2 ppm.
2-year Feeding (rat)[a]	97% Technical	NEL (systemic) = 10 ppm; no oncogenicity
2-year Feeding (dog)[a]	97% Technical	NEL (systemic) = 10 ppm
3-generation Reproduction (rat)[a]	75% Technical	NEL = 10 ppm
Delayed Neurotoxicity (hen)[a]	75% Technical	Negative at LD50 (27.5 mg/kg)
Teratology (rabbit)[c]	Technical	Negative at 1 mg/kg/day
21-day (maximum) oral cholinesterase (human)[d]	1:4 (Monitor: Orthene)	Negative at 0.1 mg/kg/day
	1:9 (Monitor: Orthene)	Negative at 0.2 mg/kg/day

a) Review by M. Quaife, 10/28/70, PP#0F0956.
b) Review by D. Ritter, 9/16/75, PP#5F1571.
c) Review by J. Doherty, 4/10/78, Reg. No.#3125-280.
d) Review by M. Quaife, 1/14/77, PP#6F1680.

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Monitor currently is not an RPAR chemical. However, in the teratology study reviewed by J. Doherty (see above), 2/63 pups had club hand, a teratologic malformation, on exposure to the highest dosage level of 3 mg/kg/day. No pups in the untreated control and the 1 mg/kg/day groups exhibited club hand.

Existing toxicity data described above, excluding studies reviewed by Ritter, were obtained by Industrial Bio-Test Laboratories, Inc. and are adequate pending validation by the registrant.

The TMRC of 0.1483 mg/day/1.5 kg computed in the accompanying printout is based on the following information from the review of M. Quaife, 10/28/70, PP#0F-0956. A 10 ppm systemic NEL in a 2-year chronic feeding study in dogs was determined, and, although a cholinesterase NEL could not be definitely established in a 90-day subacute feeding study in dogs, it was concluded that 1/10 of the lowest feeding level (1 ppm) in this subacute study would provide an ADI equal to that obtained by using a 100-fold safety factor with the 10 ppm NEL in the chronic study. In effect, therefore, the ADI in the attached printout is calculated by equating the 1ppm subacute cholinesterase "NEL" with the 10 ppm chronic systemic NEL through the use of appropriate safety factors. However, cholinesterase activity was not determined in the chronic 2-year feeding studies submitted with PP#0F0956. Regarding cholinesterase-inhibiting organophosphates such as Monitor, the ADI is ordinarily calculated from cholinesterase data obtained from 2-year chronic feeding studies and a 10-fold safety factor. Cholinesterase data from 90-day subacute studies are used to calculate the PADI based on a safety factor of 200.

Predicated on the above information, tolerances currently established for Monitor under CFR 180.315 and CFR 180.108 use up 98.86% of the ADI. Subsequently submitted 90-day subacute studies reviewed by D. Ritter (9/15/75, PP#5F1571) indicate cholinesterase NELs as high as 3 ppm in the dog and 2 ppm in the rat. However, because of the lack of cholinesterase data from 2-year chronic studies, these NELs are not being considered in the ADI calculation.

As a policy, tolerances for cholinesterase-inhibiting pesticides are not issued at levels higher than the clearly demonstrated NEL for this activity, thus assuring the absence of an acute hazard. A tolerance of 1 ppm in or on celery is currently in effect under CFR 180.108. It is recommended that the requested Section 18 usage of Monitor at 2 ppm, which exceeds the 1 ppm NOEL used to compute the ADI, not be approved.

A toxicity data requirement still outstanding is a second oncogenicity study (memo by D. Ritter, 2/24/77, PP#6E1794).

Conclusions on mutagenicity testing requirements should be deferred until Agency policy is promulgated.

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Ambush (Permethrin) alone has provided adequate control of leafminers on celery since approval for use under a Section 18 exemption in January, 1978. However, as stated in the present request, insects (including leafminers) have shown capability to build resistance to insecticides applied as single source of control instead of in combination with other insecticides. A major purpose of the present Section 18 request, therefore, is to allow the use of Monitor 4 in conjunction with Ambush to prevent increased resistance of leafminers to the latter compound.

The validity of the overall toxicity data base for Monitor is currently pending, but, taking into consideration the urgency of the request, it is concluded that the present Section 18 specific emergency exemption can be approved. However, this approval is contingent on reducing the proposed tolerance of 2 ppm to 1 ppm which equates to the level established under CFR 180.108 and the cholinesterase NEL used to calculate the ADI.

TOX/HED:th:RD Initial WDYKSTRA:7-17-79

CFR 30.315 — Monitor — 6/22/79

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ACCEPTABLE DAILY INTAKE DATA

Dog NOEL mg/kg	ppm	S.F.	ADI* mg/kg/day	MPI mg/day/60kg
0.025	1.00	10	0.0025	0.1500

Published Tolerances

CROP	Tolerance	Food Factor	mg/day/1.5kg
Broccoli(19)	1.000	0.10	0.00153
Brussel Sprouts(20)	1.000	0.03	0.00045
Cabbage,sauerkraut(22)	1.000	0.74	0.01104
Cauliflower(27)	1.000	0.07	0.00107
Cucumbers,inc pickl(46)	1.000	0.73	0.01085
Eggplant(53)	1.000	0.03	0.00045
Tomatoes(113)	1.000	2.37	0.04312
Melons(92)	0.500	2.00	0.01502
Cottonseed(11)	0.100	0.15	0.00022
Potatoes(127)	0.100	5.43	0.00814
Celery(23)**	1.000	0.29	0.00429
Lettuce(34)	1.000	1.31	0.01962
Peppers(120)	1.000	0.12	0.00134
Beans(9)**	1.000	2.04	0.03060

MPI	TMRC	% ADI
0.1500 mg/day/60kg	0.1463 mg/day/1.5kg	98.96

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*The basis for this ADI calculation may be found in the review of M. Quaife, 10/28/70, PP#0F0956. The above NOEL and SF essentially were obtained by equating a 1 ppm cholinesterase NOEL in a 90-day subacute study in dogs with a 10 ppm systemic NOEL in a 2-year chronic study in dogs through the use of appropriate safety factors.

**Tolerances contributed by Monitor as a metabolite of acephate under CFR 180.108.

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