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

APR 16 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Oxyfluorfen. List B Case No. 2490. Rohm and Haas Company 90-Day Response to Phase 4 Review. DP Barcode D171996. CBRS No. 9024.

FROM: Felecia A. Fort, Chemist
Reregistration Section II Felecia Fort
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Health Effects Division (H7509C)

THRU: William J. Hazel, Ph.D., Section Head
Reregistration Section II
Chemistry Branch II: Reregistration Support W. J. Hazel
Health Effects Division (H7509C)

TO: Bruce Sidwell/Mark Wilhite PM-53
Accelerated Reregistration Branch
Special Review/Reregistration Division (H7508W)

Rohm and Haas has submitted a 90-day response to the Phase 4 review written by Stephen Funk on March 22, 1991. Several requests have been submitted for label amendments to fulfill residue requirements on bananas/plantains, cotton, mint, and onions that will be reviewed in this memo. In addition waiver requests have been submitted to address data gaps for corn, fallow fields, and guava. Numerous studies submitted in Phase 3 by the registrant were performed by Craven Laboratories. The impact of these studies was reviewed by Stephen Funk (October 10, 1991). Their effect on reregistration will also be addressed in this memo.

Guideline # 171-4(a) Nature of the Residue - plants

Monsanto Response

The registrant has committed to conduct two new studies and would like to meet with Agency representatives to discuss plans for these studies.

Guideline # 171-4(b) Nature of the Residue - animals

Monsanto Response

The registrant committed in the Phase 3 response to supply a new study.

Guideline # 171-4 (d) Residue analytical methods - animals

Monsanto Response

Deficiencies identified will be addressed in connection with ongoing "nature of residue studies in animals."

Guideline # 171-4(e) Storage Stability

Monsanto Response

The registrant is developing storage stability data as necessary to support residue analysis of crops and animal tissues. They request a meeting, as soon as possible, with the Agency to discuss their plans for these studies.

Guideline # 171-4(j) Magnitude of the Residue in Meat/Milk/Poultry/ Eggs

Monsanto Response

The registrant has committed in the Phase 3 response to supply a new study.

Guideline # 171-4(k)

The following RACs were shown to have no data gaps pending submission of acceptable storage stability studies in the Phase 4 review; however, CBRS has recommended that a DCI be issued requiring submission of new studies to replace Craven Laboratories data as cited in "The Impact of Craven Laboratories, Inc. Analytical Data on Registrations":

> Artichoke, avocado, broccoli, figs, kiwi, pistachios, pomegranates, tree nuts

Bananas/Plantains

Data Gap: Reserved. The registrant must submit translated labels. The label information will be used to evaluate the adequacy of the reported field trials. A storage stability study is required.

Monsanto Response

The registrant submitted a translated label for the use of oxyfluorfen on bananas/plantains.

CBRS Response

The directions for use specify using 3.25 to 4.25 pints (0.65 to 0.85 lbs ai) per acre preemergence or in established plantings, post-directed for use in Puerto Rico only. A second application may be needed 90 to 100 days after first application. A 3-day PHI was stipulated.

Data collected from Mexico and Puerto Rico were analyzed by Craven Laboratories and will not be reviewed in support of reregistration. The remaining studies were conducted in Columbia and Costa Rica. One application of the 2E formulation was applied at a rate of 0.89 to 4.40 lbs ai/A with PHIs of 3, 111, and 118 days. With the exception of one sample (0.02 ppm) harvested three days after treatment at 0.89 lb ai/A, none of the samples contained any detectable residue (<0.01 ppm).

Conclusions

Deficiencies have not been resolved. Translated labels from major Central American banana-producing countries must be submitted. Additional studies are also needed. None of the data reflect the maximum seasonal application rate at the minimum PHI. One application was applied in all studies whereas label directions specify two applications. Exaggerated rate studies were conducted; however PHIs of 111 and 118 days were used (the label specifies 3 days). Two applications of the 2E formulation must be applied at 90-day intervals at the maximum label rate of 0.85 lb ai/A. A 3-day PHI must be stipulated. Additionally, these studies should be conducted in Puerto Rico and two representative Central American countries.

Cabbage

Data Gap: Additional field trials must be conducted to ensure adequate geographical representation. The tests must be conducted in WI or MI or OH, FL, and TX. A storage stability study is required for the brassica leafy vegetables.

Monsanto Response

Work will be done in cooperation with IR-4.

CBRS Response

In addition to those required in Phase 4, CBRS has recommended the issuance of a DCI requiring field trials to be conducted to replace data generated by Craven Laboratories (in NY, NJ, and GA or NC).

Cauliflower

Data Gap: Additional field trials must be conducted to ensure adequate geographical representation. The tests must be conducted in OR or WA. A storage stability study is required for the brassica leafy vegetables.

Monsanto Response

Work will be done in cooperation with IR-4.

CBRS Response

CBRS has recommended the issuance of a DCI requiring additional field trials to be conducted to replace studies performed by Craven Laboratories. Studies must be conducted in NY, MI, and FL in addition to OR or WA.

Coffee

Monsanto Response

A translocation or exaggerated rate study (5X) will be conducted as will a processing study if necessary.

Corn

Data Gap: The field trials study is acceptable, provided the registrant requests an amended PHI (60 days), provided an acceptable storage stability study is submitted for corn grain, and provided the registrant proposes acceptable corn fodder and corn forage tolerances. If the registrant intends to support the current label 30 day PHI, new field trials will be required. A processing study must be conducted for corn (field).

Monsanto Response

A waiver request was submitted for the requirements of corn. Rohm and Haas states that use of oxyfluorfen on corn is exclusively in North and South Carolina in a USDA program. The program's purpose is for the eradication of witchweed, Striga asiatica and this use

is decreasing each year. The registrant indicated that forage and fodder from treated crops are not utilized to avoid the spread of this weed.

Conclusions

The GOAL labels indicate that this use is solely for the purpose of the USDA witchweed eradication program. CBRS concurs that this use is a minor one. North and South Carolina produce only 2% of the corn grown in the United States (Agricultural Statistics, 1988). Corn is a major crop, nevertheless, and the corn grown in this program is marketable. A PHI of 60 days as well as processing studies are needed to avoid over-tolerance residues which may be found as a result of this use.

Storage stability studies are also required. Although this is a minor use and the Agency attempts to be less stringent in its requirements, if possible, by translating data from other crops, no adequate storage stability data have been submitted for any of the RACs in/on which oxyfluorfen is used. This waiver request must therefore be denied.

In regard to tolerance proposals for corn fodder and forage, restrictions are generally not allowed for field corn. Since such a proposal could negatively affect the efforts of the eradication program and since this use of oxyfluorfen is very limited, CBRS has no objection to this request.

Cotton

Data Gap: The field trial data are acceptable if the registrant intends the 90 day PHI to apply only to AZ and CA. If so, the labels must be amended to reflect clearly this intention. ALTERNATIVELY, data depicting residues of oxyfluorfen and its regulated metabolites in/on cotton seed are required. Storage stability data are required for cottonseed. The cottonseed processing data are acceptable, but storage stability data for processed commodities are required. The current cottonseed oil tolerance of 0.25 ppm must be amended based on the results of the processing study.

Monsanto Response

1. A label amendment request was submitted which states "Do not apply within 90 days of harvest for Southern cotton and within 75 days of harvest for Western Cotton".

2. A waiver is requested for the requirement to revise the cottonseed oil tolerance of 0.25 ppm since the magnitude of the concentration of residues in oil processed from field samples was described as being 3-4 fold in the processing study described in

MRID 92136075. The tolerance of 0.25 ppm is 5 fold above the tolerance of 0.05 ppm for cottonseed. Results obtained with spiked samples showing 7.5 fold concentration factor are not as reliable in predicting what the concentration factor will be in actual practice.

Conclusions

1. This deficiency is resolved. Some studies produced on cotton were generated by Craven Laboratories; however, sufficient non-Craven data are available.

2. CBRS concurs with the registrant since cottonseed oil is 33-35% of cottonseed per se affording a maximum concentration factor of 3. This is in concurrence with the results of the field weathered samples. CBRS has no objection to this waiver request.

Dates

Data Gap: A processing study must be conducted for dates. Dates with detectable residues of the parent and regulated metabolites should be processed into dried dates to determine the residue concentration or reduction factor(s). If the date trees are treated at exaggerated rates equivalent to at least the maximum theoretical concentration factor due to processing and no detectable residues are found on the rac, then processing studies are not required. Storage stability studies are required for both dates and dried dates.

Monsanto Response

Monsanto indicated that the EPA response to the Phase 3 submission does not identify what is required for dates under 171-4(k). In regard to processing studies requirements, the registrant indicated that a translocation or exaggerated rate study (2X) will be conducted as well as a processing study if necessary.

Conclusions

Initially the Phase 4 review of these studies found the studies to be acceptable for Phase 5 review pending storage stability studies. In light of the fact that all studies were conducted by Craven Laboratories, CBRS has recommended the issuance of a DCI requiring that new studies be conducted as indicated in the October 10, 1992 memo, The Impact of Craven Laboratories Analytical Data on Registrations (Stephen Funk, 10/10/91).

Fallow Field Trials

Data Gap: Data depicting residues of oxyfluorfen and the regulated metabolites in/on root and tuber vegetables, bulb vegetables, brassica vegetables, leafy vegetables, fruiting vegetables, cantaloupe, squash, watermelon, cucurbits, peanut, legume vegetables, cereal grains, celery, garlic, pepper, and tomatoes. Processing study requirements for the indicated RACs are reserved, pending results of the field trials. The general categories "Other Seed Crops" and "All Other Crops" should be removed from the label, unless the treatment to plant interval is one year or longer.

Monsanto Response

A waiver of this requirement is requested on the basis that the confined rotational crop study conducted with oxyfluorfen (MRID 40567001) provides data necessary to support the uses described in the fallow bed sections of the GOAL 1.6E label. The issue of the fallow bed use being too broad and allowing planting of crops following oxyfluorfen use which are not specifically included on the GOAL label was previously addressed by the Agency and allowed on the basis that the confined rotational crop study showed that there would be no residue in a broad range of crops planted at the intervals after GOAL application indicated in the fallow bed use directions.

CBRS Response

The confined rotational study (MRID 40567001) was conducted in Pennsylvania by Rohm and Haas. No Craven Laboratories data were submitted. Five plots were treated with [^{14}C-chlorophenyl ring] oxyfluorfen (CPR) and five were treated with [^{14}C-nitrophenyl ring] oxyfluorfen (NPR) formulated as GOAL 1.6E and applied at 1.0 lb ai/A (2X). Various crop types were included in this study including fruiting vegetables, cucurbits, root/tuber vegetables, leafy vegetables, and grain crops. Data were provided on tomatoes, pepper, squash, swiss chard, beets, turnips, collards and wheat. The crops were planted at 0, 31, 61, 91, and 123 days after application. All crops were seeded with the exception of the tomatoes, peppers and squash which were transplanted. Total ^{14}C-oxyfluorfen residues were at or below the detection limit ($\leq$0.008 ppm) except for residues found in wheat straw and chaff ($\leq$0.06ppm). Field trial data on crops for which tolerances are established indicated that residues were not detectable at rates that were at or above the maximum rate in soybeans, broccoli, and cabbage. The Phase 4 review indicated that uses on fallow beds in which cotton will be planted are anticipated to produce no greater residues than the directed application.

Treatment-to-planting intervals and use rates for various crops are indicated in the table below.

Goal Herbicide on Fallow Beds

Direct Seeded Crops	Treatment to Planting Interval (days) Use Rates:<0.25 lbs ai/A	<0.50 lbs ai/A
Carrot	90	90
Potato	60	60
Sugarbeet	60	90
Other Root/Tuber Veg.	90	90
Onions	180	180
Other Bulb Veg.	180	180
Cabbage	90	90
Cauliflower	90	90
Other Brassica Crops	120	120
Lettuce	90	120
Other Leafy Veg. except Brassica Crops	120	120
Pepper	90	120
Tomato	60	120
Other Fruiting Veg.	120	120
Cantaloupe	60	90
Squash	90	120
Watermelon	60	60
Other Curcurbits	90	120
Dry Beans	60	60
Peanuts	60	60
Soybeans	0	0
Other Legume Veg.	60	60
Cotton	14	14
Safflower	60	60
Conifer	0	0
Cereal Grains	10 months	10 months
Other Seeded Crops	180	180
Transplanted Crops		
Broccoli	0	30
Cabbage	0	30
Cauliflower	0	30
Celery	30	30
Conifer	0	0
Garlic	0	30
Grape/Kiwi	0	0
Onion	0	30
Pepper	30	30
Strawberries	30	30
Tomato	30	30
Tree fruit/Nut/Citrus	0	0
All other crops	90	180

Results of the rotation study (MRID 40567001) on various crops is presented in the following table.

Radiolabeled Oxyfluorfen Residue Levels in Rotational Crops

Crop	Sample Component	Treatment to Planting	Average ^{14}C-Oxy. Found(ppm) Int. NPR label	Total CPR label
Tomato	Fruit	0	NDR(4);0.009(1)	NDR
Pepper	Fruit	0	NDR	NDR
Squash	Fruit	0	NDR	NDR
Beets	Root	0	NDR (3);0.01(2)	NDR
Swiss Chard	Leaf	0	NDR	NDR
Spring Wheat	Grain	0	NDR	NDR
Spring Wheat	Chaff	0	NDR	NDR(3); 0.02(2)
Spring Wheat	Straw	0	0.03	0.04
Tomato	Fruit	31	NDR	NDR
Pepper	Fruit	31	NDR(4);0.01(1)	NDR(4);0.01(1)
Squash	Fruit	31	NDR	0.01
Beet	Root	31	NDR(2);0.01(3)	NDR
Swiss Chard	Leaf	31	0.01	NDR
Spring Wheat	Grain	31	NDR	NDR
Spring Wheat	Chaff	31	NDR	NDR(4); 0.04(1)
Spring Wheat	Straw	31	0.03	NDR(4); 0.02(1)
Beet	Root	61	NDR	NDR(4); 0.01(1)
Swiss Chard	Leaf	61	NDR(4); 0.01(1)	NDR
Turnip	Root	61	NDR	NDR
Collards	Leaf	61	NDR	NDR
Spring Wheat	Grain	61	NDR	NDR
Spring Wheat	Chaff	61	NDR(4);0.02(1)	NDR(4); 0.02(1)
Spring Wheat	Straw	61	0.03	0.06
Swiss Chard	Leaf	91	NDR	NDR(1); 0.01(4)
Turnips	Root	91	NDR	NDR
Collards	Leaf	91	NDR	0.01
Turnips	Root	123	NDR	NDR
Collards	Leaf	123	NDR	NDR

Note: The average ppm residue found could not be determined due to the inabiltiy to average NDR values with detectable residues for the five replicate crop combustion samples so they were reflected by the number of each NDR and detectable residue found. Single values indicate average was determined.

NDR = no detectable residues at the limit of detection of the analyses ($\leq$0.008 ppm).

Conclusions

Enough data exist to conclude that this study is acceptable for Phase 5 review; however, the phrase "All other (transplanted) crops" and "Other Seeded Crops" should be deleted from the label.

These statements are too broad. It should be noted that one or more of the following outcomes are possible from Phase 5 review (i) requiring field trials for rotational crops; (ii) requiring a proposal for tolerances (detection limit?) in/on every crop having a treatment-to-harvest interval less than one year; (iii) requiring that a 1-year treatment-to-harvest interval be associated with every use on a food/feed crop having no tolerance; and/or (iv) requiring some changes in the labeled treatment-to-planting intervals

Grapes

Monsanto Response

A translocation or exaggerated rate study (5X) will be conducted as well as a processing study if necessary.

Guava

Data Gap: A storage stability study, including data for day 0, is required for guava fruit.

Monsanto Response

A waiver request was submitted. In a letter written by IR-4, it is stated that untreated samples were spiked with a measured amount of the test substance and its metabolites, then placed in storage at the appropriate temperature until analysis and that they have never provided analytical results for Day 0. They also state that the Agency has traditionally accepted proper calculations in lieu of analytical results.

CBRS Response

Day 0 analysis is needed to provide an accurate indication of the starting amount of residues. The actual amount of decline can not be found without day 0 data. In an "ideal" situation recoveries of fortified samples result in the calculated residue amounts; however, in a "real" situation other interactions take place, i.e., sticking to sample jar, metabolic interactions, etc. In order to fully understand the stability of the chemical and/or metabolites in storage we must therefore first know what occurred when the samples were originally stored. CBRS is therefore requiring analytical results for Day 0. The data waiver is therefore denied.

Conclusions

This deficiency is not resolved. A storage stability study, including data for Day 0, is required.

Mint

Data Gap: None, provided acceptable storage stability data are supplied for mint hay, spent mint hay, and mint oil and provided the registrant intends to limit the use of oxyfluorfen to one application (1.5 lbs. a.i./acre or 2.0 lbs. a.i./acre) per season and so amends the labels. ALTERNATIVELY, new field trials, applying the 2.0 lbs. a.i./gallon or 1.6 lbs. a.i./gallon EC formulation at the maximum rate and the maximum number of applications in the minimum volume of dilution water, are required.

The current mint oil tolerance of 0.25 ppm must be amended, based on the results of the processing study.

Monsanto Response

The registrant has submitted a label amendment request on mint which limits the number of applications to one per season. The registrant has also agreed to file a tolerance petition to establish a tolerance of 1.0 ppm in mint oil.

Conclusions

This deficiency is resolved pending establishment of 1.0 ppm tolerance on mint oil.

Olive

Monsanto Response

A translocation or exaggerated rate study (5X) will be conducted as well as a processing study if necessary.

CBRS Response

Because analysis of the studies conducted on olives were performed by Craven Laboratories, CBRS has recommended that a DCI be issued requiring new field trial data be generated (as per S. Funk 10/10/91 memo) for residues of oxyfluorfen on olives along with the above studies.

Onions

Data Gap: None, pending submission of acceptable storage stability data for onions. Also, discrepancies on the label (707-174) must be corrected. The registrant must specify how many true leaves are required on the onion before treatment, three, four, or some other number. The title "Onions Grown for Seed" appears to exclude onions grown for food. This apparently is not the registrant's intention.

Monsanto Response

A label amendment request has been submitted to Joanne Miller (PM-23) of the Registration Division. The Goal 1.6E label has been changed to read as follows:

> In all states, do not start spraying until the onions have reached the minimum leaf stage specified in the "DOSAGE" section of this label. Applications made prior to the recommended onion development stage may result in serious injury and is not recommended.

Previously the label read:

> In all states, do not start spraying until the onions have four (4) fully developed true leaves. This statement conflicted with the dosage section which read "applied postemergence to seeded onions that have at least four (4) true leaves" in the case of Northeastern states and "at least three (3) true leaves" for all other states. This deficiency is resolved.

In reference to the comment made concerning "Onion Grown for Seed", the reviewer seemingly overlooked the section prior to the "Onion Grown for Seed" section which are directions for use for seeded onions.

Conclusions

The deficiency is resolved. However, CBRS has recommended that a DCI be issued requiring that new studies be submitted pursuant to deficiencies cited in the S. Funk memo (Oct. 10, 1991) concerning Craven Laboratories data submitted in support of registrations.

Pome Fruit

Data Gap: None pending submission of acceptable storage stability studies for pome fruit (apple, pear) and for apple processed commodities (fruit juice, wet pomace, dry pomace). A tolerance will be required for dehydrated apple pomace feed.

Monsanto Response

The registrant has agreed to file a tolerance petition for residues of oxyfluorfen on apple pomace feed and to fulfill the requirements for storage stability studies.

Conclusions

As a result of issues surrounding Craven Laboratories, CBRS has recommended that a DCI be issued requiring that new apple and pear field trials be conducted as well as an apple processing study, in addition to the above studies cited in the pome fruit data gap of

the Phase 4 review.

Soybean

Monsanto Response

An exaggerated rate study (5X) will be conducted as well as a processing study if necessary.

Stone fruit

Monsanto Response

The requested field trials will be conducted.

A translocation or exaggerated rate study (3X) will be conducted as well as a processing study if necessary.

CBRS Response

CBRS has recommended that a DCI be issued requiring that field trial data be generated on cherries to replace data generated by Craven Laboratories in addition to those studies cited in the Phase 4 Review.

Product Chemistry

Rohm and Haas has submitted a new study (MRID No. 41891801) to satisfy the requirements of Guideline 63-13 [Stability]. The remaining deficiency, Guideline 62-3 [Certified Limits], was not addressed.

CBRS Response

The new study (MRID No. 41891801) was reviewed by Kenneth Docktor on January 10, 1992. It was concluded that the requirement of Guideline 63-13 has been satisfied.

Conclusions:

The stability deficiency has been resolved. A deficiency still exists for Guideline 62-3 [Certified Limits].

ADDITIONAL COMMENTS

In response to comments made in the Phase 4 review of oxyfluorfen, Rohm and Haas submitted information on the requirement of Reduction of Residues. CBRS did not require any additional data; however for CBs information only here are the registrant's comments:

The Agency response to our Phase 3 oxyfluorfen submission comments that in Phase 2 we cited previously submitted studies to support this guideline but did not include them in our Phase 3 submission. The previously submitted reports cited in Phase 2 were results of residue analysis in the crops for which there are oxyfluorfen tolerances. Summaries of residue data were included in our Phase 3 response under 171-4(k) for each crop.

What the residue data show is that residues of oxyfluorfen in crops are negligible. These low levels are expected for two reasons. First, oxyfluorfen is most often applied while trees and vines are dormant. Secondly, oxyfluorfen is applied to the soil and weeds and does not translocate from soil into growing plants. Because of negligible residues on raw agricultural commodities and because often only a small percentage of a crop is treated, risks to consumers from oxyfluorfen residues are negligible, and there is no need for special procedures to further reduce or remove residues.

Furthermore, since oxyfluorfen does not translocate from soil to plants or within plants, residues found in crops must be due to surface contamination with soil or they are a result of inadvertent contamination during application. These occasional low level surface residues would be removed by normal washing or peeling.

cc(with status forms): Reviewer(F. Fort), List B File, Jay Ellenberger (SRRD)

cc (without status forms): C. Furlow(PIB/FOD), RF, SF, Circ.

RDI: WJHazel:3/12/92:EZager:4/10/92
H7509C:CBRS:CM#2:Rm800-E:FAFort/FF:2/3/92

PRODUCT CHEMISTRY

Case No.: 2490 Case Name: Oxyfluorfen
Chemical No(s).: 111601
Chemical Name(s): 2-Chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl)benzene
Registrant: Rohm and Haas Co.

Guideline Number	Is requirement applicable?	Does summary or available information indicate MRID is a candidate for Phase 5 review?	Are additional data required?	MRID Number
61-1	Y	Y	N	92136059, 92136001
61-2(a)	Y	Y[1]	N	92136059, 92136001
61-2(b)	Y	Y[1]	N	92136059, 92136001
62-1	Y	Y	N	92136059, 92136002
62-2	Y	Y	N	92136059, 92136002
62-3	Y	Y	Y[2]	92136059, 92136002
63-2	Y	Y	N	92136060C, 92136003
63-3	Y	Y	N	92136060C, 92136003
63-4	Y	Y	N	92136060C, 92136003
63-5	Y	Y	N	92136060C, 92136003
63-6	Y	Y	N	92136060C, 92136003
63-7	Y	Y	N	92136060C, 92136003
63-8	Y	Y	N	92136060C, 92136003, 92136060
63-9	Y	Y	N	92136060C, 92136003, 92136060
63-10	N[3]			
63-11	Y	Y	N	92136060C, 92136003, 92136060
63-12	N[4]			
63-13	Y	Y	N	41891801

Key: Y=yes; N=no; I=a decision cannot be made at this time; S=fully satisfies requirement; P=partially; N/A=not applicable; U=unsatisfactory.

1 MRID 41535801 contains additional manufactuing information requested (DEB No. 6085, S. Funk, 02/23/90) to evaluate the potential for halogenated dibenzo- p-dioxin/dibenzofuran formation. The submission is acceptable for review.

2 Precision and accuracy of methods used to verify certified limits of the active ingredient and impurities ($\geq$ 0.1%) must be determined and reported.

3 Registrant requests a waiver, stating that the molecular structure of oxyfluorfen is such that dissociation will not occur. CBRS agrees.

4 Registrant requests a waiver based on the low solubility of oxyfluorfen in water. CBRS agrees that pH is not a relevant property for oxyfluorfen.