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

APR 17 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#4G2987. FMC 57020 on soybeans. Evaluation of analytical method and residue data. Accession Numbers 072069, 072070, and 072071.

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THRU: Charles L. Trichilo, Chief
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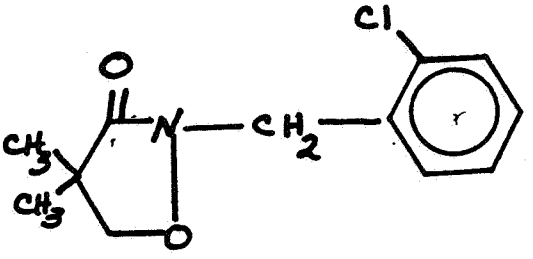
TO: Robert J. Taylor, Product Manager #25
Fungicide-Herbicide Branch
Registration Division (TS-767)

FMC Corporation, Agricultural Chemical Group, has requested the establishment of a temporary tolerance at 0.05 ppm on soybeans to cover residues of the herbicide 2-(2-chlorophenyl)-methyl-4,4-dimethyl-3-isoxazolidinone. Common and trade names have not yet been established for this new herbicide. The petitioner's code number for this compound with the following structural formula is FMC 57020.



The testing of FMC 57020 will be carried out under 279-EUP-93 and involves the use of 70,000 lbs. active on 70,000 acres of soybeans in 29 states between 3/1/85 and 3/1/86.

CONCLUSIONS AND RECOMMENDATIONS

1. For the purposes of this EUP, we consider the residue of concern in soybeans to be FMC 57020, per se.

2. An adequate analytical method is available for enforcement ses.

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3. The proposed tolerance of 0.05 ppm is adequate to cover residues of FMC 57020 which might occur on soybeans as a result of this EUP.

4. Any residues of FMC 57020 occurring in or on soybean hulls, meal, oil and soapstock as a result of this EUP will be non-detectable (<0.01 ppm).

5. Due to the absence of FMC 57020 residues in livestock feed items, and the label restriction against grazing or feeding treated vines or vine trash to livestock, no detectable residues are expected in meat, milk, and eggs from this experimental use.

Recommendation

We recommend for the proposed EUP and the establishment of a temporary tolerance of 0.05 ppm for residues of FMC 57020 (2-(2-chlorophenyl) methyl-4,4-dimethyl-3-isoxazolidinine) in or on soybeans.

The petitioner should be advised of the following requirements for a permanent tolerance on soybeans:

1. Data demonstrating that FMC 57020 residues are stable for the storage periods observed in the field trials.

2. A more complete identification of metabolites in plant material as well as a method to analyze for them if the label restriction against grazing or feeding the treated forage or hay is lifted.

3. A confirmatory method for FMC 57020 on soybeans.

4. Residue data for forage, hay and straw unless these feed items continue to be restricted.

Detailed Considerations

Manufacturing Process and Formulation

[redacted]

[redacted]

The petitioner has submitted a typical assay of the technical product:

Chemical Name	Per Cent By Weight
2-[(2-chlorophenyl)methyl]-4,4-dimethyl-3-isoxazolidinone	91.4
[redacted]	
	100.0

We would not expect any of these impurities to constitute a residue problem in view of the low levels at which they are present in the technical product.

The formulated product is an E.C. containing 50.6% technical (93% min. purity) or 4 lbs active/gallon. [redacted] All inerts have been cleared under 40 CFR 180.1001 for use on crops.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

Proposed Use

The proposed use would allow for a single preplant incorporation or preemergence application at rates of 0.5-2.0 lbs active/acre depending upon the texture of the soil. FMC 57020 will be applied using small plot sprayers, commercial ground equipment, aircraft (fixed wing, helicopter) and sprinkler irrigation. It is to be applied in a finished volume of 10 to 40 gallons of water per acre when using ground equipment or 2 to 10 gallons of water per acre with aerial equipment.

The proposed use would also allow for FMC 57020 4 EC to be used in tank mix combinations with Sencor®, Lexone®, or Lorox plus paraquat or Roundup® for preemergence (to crop and weeds) and postemergence (to weeds, but prior to crop emergence) control of broadleaf and grass weeds. All rates of each of these herbicides will be less than or up to the maximum rates for each component. All specific instructions on each product label regarding spray equipment, mixing, directions for use, methods of application, limitations and restrictions of the registered labels are to be observed.

The proposed use for FMC 52070 4 EC restricts planting any crop other than soybeans within 18 months of application. There are further restrictions against grazing livestock on treated vines, or feeding treated vines or vine trash to livestock.

Nature of the Residue

A number of studies on the fate of FMC 57020 in soybeans were submitted with this petition. Soybeans were germinated in soil treated with carbonyl-^{14}C labelled FMC 57020 or with methylene-^{14}C labelled FMC 57020 (see attached sheet for positions of the ^{14}C labels) at rates equivalent to 1 or 2 lbs active/acre.

All plants were kept in a greenhouse for the duration of this study. Plant samples were collected 30 and 60 days following treatmen Mature soybeans were harvested 116 days following treatment with carbonyl-^{14}C labelled FMC 57020 and 130 days following treatment with methylene-^{14}C labelled FMC 57020. Sample work-up included blending with methanol, filtering, concentrating under vacuum, adding water and concentrating further. The resulting aqueous fraction was centrifuged, decanted, and partitioned with methylene chloride, which yielded an organosoluble fraction, an aqueous fraction and a solid residue of plant material.

The organosoluble fraction which contained the non-conjugated products was dried over anhydrous sodium sulfate and concentrated under vacuum for chromatographic analysis.

The aqueous (polar) fraction containing the conjugated metabolites was subjected to enzyme and acid hydrolysis followed by chromatographic analyses.

The solid residue, designated as non-extractables or post-

extraction solids was assayed for total ^{14}C by combustion analysis.

The distribution of the carbonyl-^{14}C residues in the plant samples and mature soybeans receiving 2 lbs active/acre is shown in the following table:

	FRACTION	%	ppm
30 Day Plants	Non-conjugates	4.3	0.24
	Conjugates	81.1	4.57
	Aglycones	(19.4)	(1.09)
	Aqueous (Polar)	(61.7)	(3.48)
	Non-Extractables	14.6	0.82
	Total	100.0	5.63
60 Day Plants	Non-conjugates	1.8	0.02
	Conjugates	84.9	1.02
	Aglycones	(13.6)	(0.16)
	Aqueous (Polar)	(71.3)	(0.86)
	Non-Extractables	13.3	0.16
	Total	100.0	1.20
Mature Soybeans	Organosoluble	9.3	<0.01
	CH_3CN	(0.9)	(<0.005)
	Hexane	(8.4)	(0.005)
	Acid Released Organosolubles	21.3	0.01
	Aqueous (Polar)	38.1	0.02
	Bound	31.3	0.02
		100.0	0.06

The distribution of the methylene-^{14}C FMC 57020 in the plant samples receiving 2 lbs active/acre follows:

	FRACTION	%	ppm
30 Day Plants	Non-conjugates	7.9	0.83
	Conjugates	77.7	8.13
	Aglycones	(59.8)	(6.26)
	Polar	(17.9)	(1.87)
	Non-Extractables	14.4	1.51
	Total	100.0	10.47
60 Day Plants	Non-conjugates	2.9	0.15
	Conjugates	81.4	4.00
	Aglycones	(65.9)	(3.24)
	Polar	(15.5)	(0.76)
	Non-Extractables	15.7	0.68
		100.0	4.83
Mature Soybeans	Organosoluble	10.4	0.02
	CH_3CN	(0.9)	(0.00)
	Hexane	(9.5)	(0.02)
	Acid Released Organosolubles	22.9	0.04
	Aqueous (Polar)	34.7	0.05
	Bound	32.0	0.05
		100.0	0.16

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In another study, conducted to determine the level of ^{14}C residues in soybeans under actual field conditions, FMC 57020 was labeled with carbon-14 in the aromatic ring and the carbonyl carbon of the isoxazolidinone ring. Four individual test plots were treated with a single soil application: two received a 2 lb or a 3 lb ai/acre application, respectively, of carbonyl ^{14}C FMC 57020 and two received a 2 lb or a 3 lb ai/acre application, respectively, of ring $-^{14}C$ FMC 57020. Soybean plants were randomly sampled at 30 and 58 days from each test plot. Mature soybean samples were collected 118 days following treatment. The radiolabeled residues found in 30 and 58 day plant samples and mature soybeans are shown below:

	2 lb ai/a			3 lb ai/a		
	30 (days)	58 (days)	Soybean (mature)	30 (days)	58 (days)	Soybean (Mature
	ppm	ppm	ppm	ppm	ppm	ppm
carbonyl-^{14}C FMC 57020	3.52	0.74	0.10	3.60	1.40	0.15
ring-^{14}C FMC 57020	2.39	0.70	0.10	3.73	1.40	0.23

Soybeans from all of the above studies were analyzed for total $^{14}-C$ residues. The results of that study are shown in the table below:

	Field (Outdoor)				Greenhouse (Indoor)			
$^{14}-C$ Label	Carbonyl-$^{14}-C$		Ring-$^{14}-C$		Carbonyl-$^{14}-C$		Ring-$^{14}-C$	
Applic. Rate (lb ai/a)	2	3	2	3	1	2	1	2
Total Residue (ppm)	0.10	0.15	0.10	0.23	0.04	0.06	0.11	0.16

Soybeans which received 2 lb ai/a from the different labelled studies were subjected to solvent extraction (see attached sheet of general outline for solvent extraction of soybeans) followed by acid hydrolysis. Characterization of the residue involved combining fractions of a similar nature i.e., ethyl acetate soluble metabolites, polar metabolites, and bound residue, and determining the final distribution of $^{14}-C$ residues from 2 lb ai/a in the various fractions as shown in the following table:

	Outdoor				Greenhouse			
	Carbonyl-$^{14}-C$		Ring-$^{14}-C$		Carbonyl-$^{14}-C$		Methyl-ene-$^{14}-C$	
Fraction	%	ppm	%	ppm	%	ppm	%	ppm
Hexane Solubles	10.6	0.01	12.6	0.01	9.8	0.01	9.9	0.02
	1.4	0.00	2.1	0.00	0.7	0.00	0.5	0.00
Ethyl Acetate Solubles	27.8	0.03	47.7	0.05	24.4	0.01	22.9	0.04
Polar Metabolites	38.4	0.04	18.9	0.02	41.1	0.02	34.7	0.05
Bound Residue	21.8	0.02	18.7	0.03	24.0	0.01	32.0	0.05
Total	100.0	0.10	100.0	0.11	100.0	0.05	100.0	0.16

The petitioner made further attempts to isolate and identify the metabolites of FMC 57020. Fractionation of ring-^{14}C labelled FMC 57020 treated soybeans grown outdoors using either 2 or 3 lbs active/acre resulted in 47.7% and 48.0%, respectively, of the total ^{14}-C residues to be ethyl acetate solubles. The combined ethyl acetate solubles (Fractions VII and X) were evaporated, treated with methylene chloride, and fractionated through activated silica-gel Sep-Paks. Fractions were further purified with gel permeation chromatography and thin layer chromatography. Further analysis of the TLC purified metabolites using high pressure liquid chromatography showed seven metabolites, of which three were tentatively identified. The HPLC chromatographic distribution of purified ring-^{14}C organosoluble metabolites are as follows:

Fraction	2 lb ai/a %	2 lb ai/a ppm	3 lb ai/a %	3 lb ai/a ppm
o-Chlorobenzyl Alcohol	5.2	(0.01)* 0.00	12.1	(0.03)* 0.02
Hydroxy-o-Chloro-benzyl Alcohol(s)**	19.0	(0.02) 0.01	10.8	(0.02) 0.02
o-chlorobenzoic acids***	0.8	(0.00) 0.00	1.3	(0.00) 0.00
Unknowns/4	2.8	(0.00)	2.1	(0.00)
Remaining Unanalyzed Residue	19.9	(0.02)	21.8	(0.05)
Total	47.7	(0.050)	48.0	(0.10)

* FMC 57020 equivalent

** Fraction assumed to be a mixture of 3 possible hydroxylated o-chlorobenzyl alcohol isomers.

*** Fractions assumed to be a mixture of o-chlorobenzoic acid and hydroxy-o-chlorobenzoic acid(s), based on similar HPLC retention times of known analytical standards.

From the submitted studies it can be concluded that FMC 57020 is absorbed from the soil through the root structure and translocated into the immature plant. Residue levels declined in the plant with time. Beans from plants germinated in soil treated with 2 lb ai/a of methylene ^{14}C FMC 57020 showed residue levels of 0.16 ppm at harvest while mature beans from plants grown in soil treated with 2 lb ai/a of carbonyl ^{14}C FMC 57020 showed levels of approximately 0.06 ppm. Approximately 80% of the residue in the immature plant is polar conjugated metabolites. In the mature bean between 65-70% of the ^{14}C residue is polar or bound to plant solids. Considering the low levels of activity found in mature soybeans we are willing to conclude for the purposes of this EUP that parent FMC 57020 is the residue of concern.

The petitioner should be advised that if the restrictions against grazing or feeding treated forage or hay are lifted, we will require a more complete identification of metabolites in the plant material as well as a method to analyze for them.

Analytical Method

The analytical method used in generating the data for this submission entails acid hydrolysis of the sample, extraction of the FMC 57020 residues with hexane, a sodium bicarbonate wash, followed by Florisil column chromatography, and quantitated using gas chromatography-mass spectrometry (GC/MS) in a selected ion monitoring mode.

This method is modified slightly when analyzing for FMC 57020 residues in soybean oil and soapstock. Here, the sample is mixed in hexane and aqueous acid solutions. The hexane solution is collected and washed with a solution of sodium bicarbonate and then partitioned with acetonitrile to recover FMC 57020 from the hexane. Water is added to the acetonitrile and the aqueous acetonitrile is partitioned with hexane. The hexane solution is then cleaned up further on a Florisil column for GC/MS analysis.

This method was utilized to measure residues of parent FMC 57020 only. Method sensitivity in all soybean samples was established to be 0.05 ppm. Method detectability was claimed to be 0.01 ppm.

Recovery data were submitted for unprocessed soybeans, soybean hulls, solvent-extracted soybean meal, crude soybean oil, refined soybean oil, and soapstock at fortification levels of 0.05 ppm, 0.10 ppm, and 0.20 ppm. Recoveries ranged from 70% to 110%. All control values were non-detectable (<0.01 ppm).

We consider the above method adequate for enforcing a temporary tolerance of 0.05 ppm for the herbicide FMC 57020 *per se*.

A confirmatory method will be needed for permanent tolerances.

Residue Data

To this point we have not received storage stability data for this herbicide. Since the trials do not state the actual dates of analysis, we are unable to determine how long samples were stored. For a permanent tolerance we will require data demonstrating that FMC 57020 are stable for the storage periods observed in field trials.

Residue data with FMC 57020 on soybeans from 24 studies conducted

in nine states were submitted with this petition. In half of the studies, FMC 57020 was applied as a preplant incorporated (PPI) treatment while the remaining half received a pre-emergence (PRE) treatment. All application rates were 2.0 lbs ai/a, the maximum proposed rate. Mature soybean samples were harvested at 111 to 152 days after either the PPI or PRE application treatment. There were no detectable residues of FMC 57020 in any soybean sample analyzed.

These data are adequate to support the requested 0.05 ppm tolerance for residues of FMC 57020 on soybeans.

There was no submission of residue data on soybean forage, hay and straw. At this time no residue data or tolerance proposals are necessary on these feed items since the proposed label restricts grazing livestock on treated vines or feeding treated vines or vine trash to livestock.

The petitioner has submitted a processing study to determine the concentration of FMC 57020 residues in soybean hulls, solvent-extracted soybean meal, crude soybean oil, refined-deodorized-bleached -soybean oil, and soybean soapstock. These processed commodities were from mature soybeans which had received broadcast pre-emergence treatment of 3.0 lb ai/a and were harvested 139 days later.

There were no detectable FMC 57020 (<0.01 ppm) in the unprocessed beans or in any processed soybean fraction.

The petitioner should be advised of the following requirements for a permanent tolerance on soybeans:

1. A more complete identification of metabolites in plant material as well as a method to analyze for them if the label restriction against grazing or feeding treated forage or hay are lifted.

2. Residue data for forage, hay and straw unless these feed items continue to be restricted.

Meat, Milk, Poultry and Eggs

Considering that no detectable residues of FMC 57020 *per se* are expected in soybeans or its byproducts and that forage, hay and straw are restricted, we have no objections to the absence of livestock metabolism and feeding studies of this herbicide. No detectable residues are expected in meat, milk, poultry and eggs.

cc: R.F., Circ., Reviewer, TOX, EEB, EAB, PP#4G2987, FDA
Robert Thompson
RDI: A.R.Rathman:4/16/84:R.D.Schmitt:4/17/84
TS-769:L.S.Propst:lsp:Rm810:4/17/84

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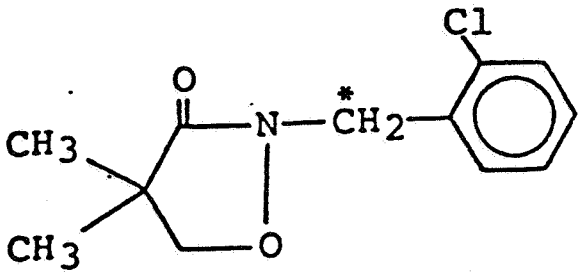
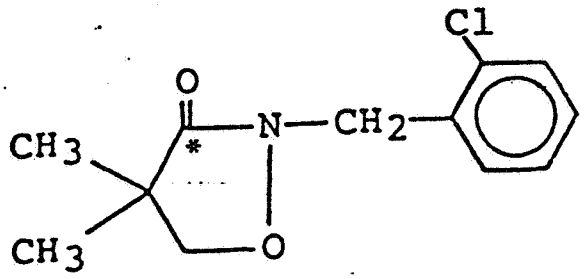
FMC 57020

^{14}C-LABELED CHEMICALS



METHYLENE-^{14}C FMC 57020



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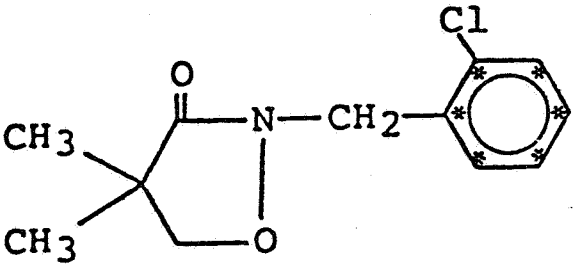

RING-^{14}C FMC 57020

*DENOTES ^{14}C-LABEL

EXTRACTION OF SOYBEANS