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

OCT 12 1995

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: PP No. 5F4541: New Chemical: Azoxystrobin (ICIA5504) in/on Grape RAC's and Rotational Crops. Issues to be Presented to HED's Metabolism Committee. DP Barcode D218448 CBTS Nos. 16051 and 16092

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THRU: M. Metzger, Chief
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TO: HED Metabolism Committee

Zeneca Ag Products, Wilmington, DE has petitioned the Agency for the registration of and for permanent tolerances resulting from the use of azoxystrobin as a fungicide on grapes. The petitioner requests tolerances of 1 ppm of the parent in/on grapes, 2 ppm in/on dry grape pomace, and 9 ppm in/on raisin waste.

Azoxystrobin (BSI), methyl (E)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate, is related to naturally occurring strobilurins. It is a new chemical with no prior registrations.

At a pre-registration meeting (4/25/95), the petitioner summarized the available metabolism data and requested that this data be presented to the HED Metabolism Committee for a determination of the residue of concern. The metabolism data discussed at this meeting was provided to the Agency on May 29, 1995 and is the basis for the presentation and discussion in this memo.

Since that time, a request for the registration of azoxystrobin and for permanent tolerances on grapes has been submitted to the Agency (PP#5F4541). Data from this petition will be utilized in this memo, as needed, to provide details of the material presented in summary at the April meeting. Structures of azoxystrobin (ICIA 5504) and its metabolites are shown on the last two pages of this memo. Note that compound numbers such as 2 and 28 in the figure of

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biotransformations are equivalent to 5504/2 and 5504/28 of the table for rotational crops.

Nature of the Residue in Plants

Grapes

Site: Toulouse, France

Material Applied: Azoxystrobin labeled in either the cyanophenyl ring, the pyrimidinyl ring, or the phenylacrylate ring

Application Rate: Four applications during growing season, totaling the equivalent of 2.4 to 2.6 lbs ai/A.

PHI: Twenty-one days (The proposed label has a 14 day PHI.)

Results: TRR: labeled cyanophenyl ring 0.382 ppm
labeled pyrimidinyl ring 1.43 ppm
labeled phenylacrylate ring 0.951 ppm

Nature of residue: Sixty-two to seventy-nine percent of the residue was identified

Azoxystrobin (and its isomer, Compound 9) was the major component accounting for 34 to 66% of the TRR

Ten other metabolites were identified with Compound 13 accounting for 5.7 % of the TRR

Wheat (from summary provided of this study)

Site: Jealott's Hill, UK

Material Applied: Azoxystrobin labeled in either the cyanophenyl ring, the pyrimidinyl ring, or the phenylacrylate ring

Application Rate: Two applications during growing season, totaling the equivalent of 0.9 to 1.0 lbs ai/A.

PHI: Thirteen days for forage
Sixty-one or sixty-two days for grain and straw

Results: Grain

TRR: labeled cyanophenyl ring 0.075 ppm
labeled pyrimidinyl ring 0.077 ppm
labeled phenylacrylate ring 0.076 ppm

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Wheat (continued)

Forage

TRR:	labeled cyanophenyl ring	2.79	ppm
	labeled pyrimidinyl ring	1.02	ppm
	labeled phenylacrylate ring	2.14	ppm

Straw

TRR:	labeled cyanophenyl ring	9.41	ppm
	labeled pyrimidinyl ring	3.08	ppm
	labeled phenylacrylate ring	7.22	ppm

Nature of residue: Azoxystrobin (and its isomer, Compound 9) was the major component in all commodities accounting for 17 to 65% of the TRR

Fourteen other metabolites were identified of which one (Compound 28) accounted for 10 percent of the TRR All others were present at less than 5% of the TRR

Peanuts (from summary provided of this study)

Site: Visalia, CA

Material Applied: Azoxystrobin labeled in either the cyanophenyl ring, the pyrimidinyl ring, or the phenylacrylate ring

Application Rate: Three applications during growing season, totaling the equivalent of 1.8 lbs ai/A.

PHI: Ten days for vines, hay, hulls, and nuts

Results: Nutmeat

TRR:	labeled cyanophenyl ring	0.24	ppm
	labeled pyrimidinyl ring	0.65	ppm
	labeled phenylacrylate ring	0.49	ppm

Hulls

TRR:	labeled cyanophenyl ring	0.75	ppm
	labeled pyrimidinyl ring	0.87	ppm
	labeled phenylacrylate ring	0.68	ppm

Peanuts (continued)

Hay

TRR:	labeled cyanophenyl ring	40.2	ppm
	labeled pyrimidinyl ring	39.2	ppm
	labeled phenylacrylate ring	46.6	ppm

Vines

TRR:	labeled cyanophenyl ring	17.4	ppm
	labeled pyrimidinyl ring	16.4	ppm
	labeled phenylacrylate ring	19.8	ppm

Nature of residue: In nutmeats no metabolites were present at 0.01 ppm. The radiolabel was found in fatty acids and sugars.

Azoxystrobin (and its isomer, Compound 9) was the major component of residues in hay and vines accounting for 33 to 45% of the TRR

Fourteen other metabolites were identified as present at less than 5% of the TRR

Confined Rotational Crops

Site: Richmond, CA

Material Applied: Azoxystrobin labeled in labeled in either the cyanophenyl ring, the pyrimidinyl ring, or the phenylacrylate ring

Application Rate: Soil in pots treated with 1.8 lbs ai/A equivalent. Crops (lettuce, radishes, wheat) planted 30, 200, and 365 days after treatment. (Soil residue determined as 1.0 lbs ai/A at 30 days) Petitioner calculates rate of application as a 40 x exaggeration of level of residues that would be expected at suggested use rates and field conditions.

PHI: Conventional for rotational crops.

Results: Total residues as ppm of azoxystrobin

CROP	30 DAT			200 DAT			365 DAT		
	Cyano	Pyr	PA	Cyano	Pyr	PA	Cyano	Pyr	PA
Lettuce	0.43	0.28	0.15	0.11	0.10	0.03	0.03	0.4	<0.01

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Results: (continued) Total residues as ppm of azoxystrobin

CROP	30 DAT			200 DAT			365 DAT		
	Cyano	Pyr	PA	Cyano	Pyr	PA	Cyano	Pyr	PA
Radish Top	0.76	1.09	0.49	0.29	0.52	0.14	0.05	0.04	0.04
Radish Root	0.16	0.19	0.12	0.05	0.10	0.04	0.02	<0.01	0.01
Wheat Forage	2.16	2.34	1.18	0.42	0.62	0.16	0.09	0.11	0.03
Wheat Straw	13.0	15.2	5.92	2.92	2.47	0.66	0.46	0.38	0.13
Wheat Grain	0.20	0.33	0.16	0.07	0.11	0.03	0.03	0.03	<0.01

Nature of the residue:

In 30 DAT crops, the petitioner could account for 61% (wheat grain) to 99% (lettuce) of the applied radioactivity, and could identify 8% (wheat grain) to 91% (lettuce) of the residue. In the 30 DAT crops, 1.8% (radish tops) to 27% (radish roots) of the TRR was identified as azoxystrobin.

The petitioner has supplied the table that follows that shows the % of the TRR found in rotational crops planted 30 and 200 days after treatment of the soil.

Depending on the crop, metabolites of azoxystrobin i.e., Compounds 42, N1/N2, O2, O3, and G2 were found at higher levels than azoxystrobin itself.

Animal Metabolism

In the rat metabolic study, Compounds 2, 13, 28, and their conjugates were found. Azoxystrobin and its isomer Compound 9 were not found. The summary provided to CBTS gives no indication as to whether other plant metabolites were found in the rat.

Residue of Concern

On the bases of these studies the petitioner has proposed the residue of concern in plants as azoxystrobin and its Z-isomer (Compound 9)

Questions for Metabolism Committee to Consider:

Should the residue of concern in grapes as a primary crop be considered azoxystrobin and its Z-isomer for both enforcement purposes and dietary risk assessment?

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Should the residue of concern in rotational crops be considered azoxystrobin and its Z-isomer only or should the metabolites (Compounds 42, N1/N2, O2, O3, and G2) occurring at higher levels than azoxystrobin also be considered as of concern in rotational crops?

Attachments: Structures of azoxystrobin and its metabolites with postulated metabolic pathways.

cc: R.F.; Circ.; Garbus; PP#5F4541
RDI:RAL:10/12/95:MSM:10/12/95
H7509:CBTS:JG:jg:10/12/95:CM#2:805c:305-5405

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Pages 9 through 10 are not included.

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