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

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Atrazine/Review # 52/11.4.83/8 pages Releasable

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Subject: PP 3F2870. Atrazine on rangegrass. Evaluation of analytical methods and residue data.

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Thru: Charles L. Trichilo, Chief
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To: Robert Taylor, PM 25
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

Ciba-Geigy Corporation is proposing changing the spring application rate of atrazine [2-chloro-4-ethylamino-6-(isopropylamino)-s-triazine] from 1 lb ai/A to 2 lb ai/A on rangegrass while reducing the PHI from 3 months to 2 months. The registrant claims that the established tolerance of 4 ppm for atrazine and three of its chloro metabolites will be adequate for the changed use. No change is proposed for the registered fall application to rangegrass.

Conclusions

1a. The nature of the residue in plants is considered to be atrazine and its dealkylated chloro metabolites.

1b. A large ruminant metabolism study is needed to determine the nature of the residue in livestock other than poultry.

2a. Analytical methods are available for atrazine and its three dealkylated chloro metabolites.

2b. Depending on the results of the metabolism study requested in 1b. above, additional methodology may be needed.

3. Total residues are likely to exceed the existing 4 ppm tolerance on rangegrass from the amended use for spring application. A more appropriate tolerance of 15 ppm should be proposed.

4a. Residues of atrazine *per se* are not likely to exceed the established tolerances in animal tissues and milk. Depending on the results of the metabolism study requested in 1b. above, a new feeding study may be needed to determine the total residue in animal tissues and milk.

4b. There are no poultry feed items in this proposal, therefore there will be no proplem of secondary residues in poultry and eggs from this use.

5. The International Residue Limit Status sheet is attached. There are no Codex, Canadian or Mexican residue limits for atrazine on this crop.

Recommendations

We recommend against the proposed amended use because of Conclusions 1b., 2b., 3 and 4a.

Detailed Considerations

Nature of the Residue

The metabolism of alkylamino chloro- and methyl thio-triazines have been discussed in previous reviews of PP 4F1425 (atrazine), PP OF0996 (simazine) and PP 2F2618 (propazine). Numerous articles dealing with the metabolism of these compounds have been published and a summary of various studies is submitted (Esser, et al, "s-Triazines," Herbicides - Chemistry, Degradation, and Mode of Action, Kearney, P. C. and Kaufman, D. D., edit., Vol. 1, Chapter 2, pp. 129-208. Marcel Dekker, Inc. 1975).

Depending on the plant species and stage of growth, the predominate metabolic pathway may be conjugate formation, hydroxylation and/or N-dealkylation. Conjugation with glutathione and gamma-glutamylcysteine occurs in many mono-cotyledonous plants as does formation of hydroxy atrazine. Formation of both deethylated and deisopropylated atrazine has been noted; dealkylation may either follow or precede hydroxy formation. The three tolerated plant metabolites are 2-amino-4-chloro-6-ethylamino -s-triazine (G-28279), 2-amino-4-chloro-6 -isopropylamino-s-triazine (G-30033) and 2-chloro-4,6-diamino-s-triazine (G-28273).

We consider the nature of the residue in plants to be adequately understood.

Only summaries of animal metabolism studies are submitted.

Two pathways of atrazine metabolism in animals are N-dealkylation and glutathione conjugation at the chloro group leading to mercapturic acid end products. When animals were fed side-chain labeled atrazine, over 50% of the activity was evolved as $^{14}CO_2$. Mono and didealkylated s-triazine compounds have been found in the urine of rats and rabbits from feeding nonlabeled atrazine, simazine, propazine, prometone, and prometryn. The corresponding 2-hydroxy compounds have been identified in the urine of rats treated with radiolabeled atrazine. Ammeline, the hydroxy diamino derivative, has been found in rat and cow urine after application of atrazine. Further degradation to amelide and cyanuric acid occur when the mono and didealkyated compounds are fed.

No large ruminant or poultry metabolism study is available characterizing the animal residues in tissues although in general the metabolic pathway is known.

The registration standard for atrazine states that studies are required to determine the nature of the residue in food animals. The present proposal will require a substantial increase in the tolerance on rangegrass (see Residue Data), therefore we concur with the registration standard that a large ruminant metabolism study is needed.

Analytical Methods

Analytical methods are available for the parent compound and the chloro metabolites. Successful method trials have been conducted for simazine and its mono-dealkylated chloro metabolite (method AG-213) and validation data submitted for atrazine and its mono-dealkylated chloro metabolite by a similar method, AG-262. A successful method trial was conducted for G-28273, the di-dealkylated chloro metabolite (method AG-232A), common to propazine, atrazine, and simazine, in connection with PP#2F2618.

Depending on the results of the requested animal metabolism studies, additional methodology for other metabolites may be needed.

Residue Data

Six additional residue studies for atrazine on rangegrass were submitted in this petition. Altogether, ca 35 studies have been submitted for spring application of 2 lb atrazine/A on rangegrass in 7 states in the midwest and Florida (see also PP4F1425 and amended registration submission of 1978). The PHIs range from 0 days to over a year. An analysis of this data show that the residues vary so greatly even between replicate samples that they do not fit a normal decline curve. The data show an initial rapid drop in residue of the parent compound with a gradual rise in metabolite residues.

Maximum residues are as follows:

	PHI (days)	Green forage	Hay
Atrazine	0	315	511
	60	6.7	1.8
	90	0.5	0.4
Metabolites	30	5.1	5.7
	60	2.8	9.4
	99	1.9	2.9

The petitioner states that the maximum residues are from an area in Texas with low rainfall and that use in that area will be prohibited on the label because of phytotoxicity. However, we cannot ignore this data because tolerances are not as a rule set for particular geographical locations and seasons of low rainfall could account for over tolerance residues in other locations.

We conclude that residues are likely to exceed the established tolerance of 4 ppm from the proposed use of 2 lb ai/A with a 2 month PHI. We feel that a more appropriate tolerance of 15 ppm, as for orchardgrass and corn forage, should be proposed.

Meat, Milk, Poultry and Eggs

There are no poultry feed items in this proposal, therefore there will be no proplem of secondary residues in poultry or eggs.

The existing meat and milk tolerances will cover any secondary residues of atrazine per se generated by this use.

No conclusions can be made regarding the levels of atrazine metabolites which might be present in meat and milk as a result of this use. Depending on the results of the requested metabolism study, a new large reminant feeding study may be needed.

TS-769:RCB:MBradley: :CM#2:Rm810:5577377:10/31/83
cc: RF, Circ., Bradley, Thompson, FDA, TOX, EEB, EFB, PP#3F2870
RDI: Quick,11/1/83; Schmitt,11/1 /83

1E; BRADLEY

TLE: PP3F2870

MARKS: ATRAZINE SPRING GREEN 2LB/A

LE NAME: ATRSP

RESIDUE LEVELS IN PPM

INTERVALS IN DAYS

TA ENTRIES 1 TO 111

15 at 0 DAYS	97 at 0 DAYS	.1 at 37 DAYS	.05 at 62 DAYS
15 at 0 DAYS	83 at 0 DAYS	.36 at 43 DAYS	.05 at 62 DAYS
11 at 0 DAYS	64 at 0 DAYS	1.6 at 55 DAYS	.05 at 62 DAYS
90 at 0 DAYS	38 at 1 DAYS	.06 at 58 DAYS	.05 at 62 DAYS
86 at 0 DAYS	36 at 1 DAYS	.15 at 59 DAYS	4.1 at 63 DAYS
75 at 0 DAYS	120 at 7 DAYS	.05 at 59 DAYS	1.5 at 63 DAYS
65 at 0 DAYS	5 at 14 DAYS	6.7 at 60 DAYS	1.3 at 63 DAYS
64 at 0 DAYS	1.7 at 21 DAYS	4.8 at 60 DAYS	1.2 at 63 DAYS
253 at 0 DAYS	25 at 30 DAYS	4.4 at 60 DAYS	.05 at 65 DAYS
230 at 0 DAYS	8 at 30 DAYS	2.5 at 60 DAYS	.05 at 65 DAYS
225 at 0 DAYS	.31 at 30 DAYS	1.2 at 60 DAYS	.48 at 90 DAYS
218 at 0 DAYS	.27 at 30 DAYS	1 at 60 DAYS	.4 at 90 DAYS
214 at 0 DAYS	.2 at 30 DAYS	.84 at 60 DAYS	.38 at 90 DAYS
204 at 0 DAYS	.14 at 30 DAYS	.58 at 60 DAYS	.26 at 90 DAYS
203 at 0 DAYS	25 at 31 DAYS	.42 at 60 DAYS	.05 at 90 DAYS
202 at 0 DAYS	16 at 31 DAYS	.42 at 60 DAYS	.05 at 90 DAYS
199 at 0 DAYS	5 at 31 DAYS	.38 at 60 DAYS	.05 at 90 DAYS
173 at 0 DAYS	1.8 at 31 DAYS	.05 at 60 DAYS	.05 at 91 DAYS
168 at 0 DAYS	.05 at 31 DAYS	.05 at 60 DAYS	.05 at 91 DAYS
158 at 0 DAYS	.44 at 32 DAYS	.05 at 60 DAYS	.05 at 91 DAYS
143 at 0 DAYS	.44 at 32 DAYS	.05 at 60 DAYS	.05 at 91 DAYS
139 at 0 DAYS	.13 at 35 DAYS	.05 at 60 DAYS	.26 at 92 DAYS
130 at 0 DAYS	.06 at 35 DAYS	.05 at 60 DAYS	.21 at 92 DAYS
126 at 0 DAYS	.05 at 35 DAYS	.19 at 61 DAYS	.31 at 99 DAYS
123 at 0 DAYS	.05 at 35 DAYS	.16 at 61 DAYS	.27 at 99 DAYS
117 at 0 DAYS	.05 at 35 DAYS	.05 at 61 DAYS	.08 at 320 DAYS
114 at 0 DAYS	.05 at 35 DAYS	.05 at 61 DAYS	.05 at 380 DAYS
112 at 0 DAYS	.27 at 37 DAYS	.17 at 62 DAYS	

REMARKS: METABOLITES GREEN FORAGE 2LB/A

FILE NAME: AZMETG

RESIDUE LEVELS IN PPM

INTERVALS IN DAYS

DATA ENTRIES 1 TO 70

2.85 at 30 DAYS	.06 at 37 DAYS	.1 at 60 DAYS	.68 at 90 DAYS
2.46 at 30 DAYS	.44 at 43 DAYS	.1 at 60 DAYS	.57 at 90 DAYS
.51 at 30 DAYS	.43 at 58 DAYS	.08 at 60 DAYS	.55 at 90 DAYS
.41 at 30 DAYS	.14 at 59 DAYS	.33 at 61 DAYS	.1 at 90 DAYS
5.1 at 31 DAYS	.1 at 59 DAYS	.24 at 61 DAYS	.13 at 91 DAYS
3.72 at 31 DAYS	1.82 at 60 DAYS	.54 at 62 DAYS	.1 at 91 DAYS
.87 at 31 DAYS	1.07 at 60 DAYS	.1 at 62 DAYS	.1 at 91 DAYS
.83 at 31 DAYS	1.06 at 60 DAYS	.1 at 62 DAYS	1.12 at 92 DAYS
.25 at 31 DAYS	1.06 at 60 DAYS	.1 at 62 DAYS	.98 at 92 DAYS
.17 at 32 DAYS	.83 at 60 DAYS	.07 at 62 DAYS	1.93 at 99 DAYS
.09 at 32 DAYS	.55 at 60 DAYS	2.84 at 63 DAYS	1.46 at 99 DAYS
.32 at 35 DAYS	.51 at 60 DAYS	2.53 at 63 DAYS	.2 at 115 DAYS
.27 at 35 DAYS	.3 at 60 DAYS	1.45 at 63 DAYS	.1 at 116 DAYS
.14 at 35 DAYS	.24 at 60 DAYS	1.24 at 63 DAYS	.18 at 122 DAYS
.12 at 35 DAYS	.22 at 60 DAYS	.1 at 65 DAYS	.18 at 124 DAYS
.1 at 35 DAYS	.22 at 60 DAYS	.1 at 65 DAYS	.25 at 153 DAYS
.09 at 35 DAYS	.17 at 60 DAYS	2.3 at 90 DAYS	
.22 at 37 DAYS	.15 at 60 DAYS	1.18 at 90 DAYS	

AME: BRADLEY

DATE: 10/26/83

ITLE: PP3F2870 ATRAZINE ON RANGEGRASS

EMARKS: ATRAZINE SPRING HAY 2LB/A

ILE NAME: ATRHAY

RESIDUE LEVELS IN PPM

INTERVALS IN DAYS

ATA ENTRIES 1 TO 39

511 at 0 DAYS	4.4 at 30 DAYS	.05 at 60 DAYS	.1 at 91 DAYS
511 at 0 DAYS	24 at 31 DAYS	.4 at 61 DAYS	.05 at 91 DAYS
435 at 0 DAYS	19 at 31 DAYS	.37 at 61 DAYS	.05 at 92 DAYS
405 at 0 DAYS	6.6 at 31 DAYS	1.8 at 63 DAYS	.05 at 92 DAYS
206 at 0 DAYS	2.8 at 31 DAYS	1.3 at 63 DAYS	.37 at 99 DAYS
145 at 0 DAYS	1.5 at 32 DAYS	1.1 at 63 DAYS	.36 at 99 DAYS
95 at 0 DAYS	.85 at 32 DAYS	.82 at 63 DAYS	.1 at 320 DAYS
74 at 0 DAYS	.5 at 43 DAYS	.05 at 90 DAYS	.14 at 380 DAYS
45 at 0 DAYS	5 at 55 DAYS	.05 at 90 DAYS	.06 at 440 DAYS
9.1 at 30 DAYS	.08 at 60 DAYS	.13 at 91 DAYS	

REMARKS: METABOLITES HAY SPRING 2LB/A

FILE NAME: AZMETH

RESIDUE LEVELS IN PPM

INTERVALS IN DAYS

DATA ENTRIES 1 TO 22

4.37 at 30 DAYS	.45 at 32 DAYS	9.39 at 63 DAYS	.1 at 91 DAYS
3.76 at 30 DAYS	.32 at 32 DAYS	6.22 at 63 DAYS	.1 at 92 DAYS
5.7 at 31 DAYS	.35 at 43 DAYS	1.52 at 63 DAYS	2.85 at 99 DAYS
5.19 at 31 DAYS	.06 at 60 DAYS	1.43 at 63 DAYS	2.52 at 99 DAYS
.45 at 31 DAYS	.31 at 61 DAYS	.1 at 90 DAYS	
.34 at 31 DAYS	.23 at 61 DAYS	.1 at 91 DAYS	

CHEMICAL Atrazin

PETITION # PP#3F2870

10/28/83

L.L.

CCPR NO. none

Codex Status

☑ No Codex Proposal Step 6 or above

Proposed U. S. Tolerances

Residue (if Step 9): _____

Residue: Atrazine and its three chloro-metabolites

Crop(s)	Limit (mg/kg)

Crop(s)	Tol. (ppm)
Rangegrass	4

CANADIAN LIMIT

Residue: _____

Crop	Limit (ppm)
none (on range grass)	

MEXICAN TOLERANCIA

Residue: _____

Crop	Tolerancia (ppm)
None (on range gress)	

Notes: