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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE:

SUBJECT:

PP#1F2506. Metolachlor in Cottonseed.
Evaluation of residue data and analytical method.

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The CIBA-GEIGY Corporation proposes a tolerance for combined residues of the herbicide metolachlor, 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl) acetamide, and its metabolites 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone, (each expressed as metolachlor), in or on cottonseed at 0.1 ppm.

Permanent tolerances are established for metolachlor in corn grain (except popcorn) at 0.1 ppm; soybeans at 0.1 ppm; peanuts at 0.1 ppm, peanut hulls at 1.0 ppm, and peanut forage and hay at 3 ppm (PP#9F2213); sorghum grain at 0.3 ppm and sorghum forage and fodder at 2.0 ppm; and, eggs, milk, meat, fat, and meat byproducts of livestock at 0.02 ppm (§180.368).

Tolerances are pending for metolachlor residues in sunflower seed at 0.3 ppm (PP#OE2416), flax at 0.2 ppm (PP#OE2417), and seed and pod vegetables at 0.3 ppm (PP#1F2495).

Conclusions

1. The nature of the residue in plants and animals is adequately understood. The significant components of the residues are the parent metolachlor and its metabolites as noted above.
2. Adequate analytical methods are available for enforcement purposes.
- 3a. Residues in cottonseed or its byproducts (hulls, meal, oil, soapstock) are not likely to exceed the proposed tolerance.
- 3b. Residues of prometryne or fluometuron in cottonseed are not likely to exceed the established tolerances due to the tank-mix uses.
4. Residues of metolachlor could occur in eggs, milk, and meat of livestock [§180.6 (a)(2)]; however, such residues would be adequately covered by the established tolerances.

Recommendation

TOX considerations permitting, we can recommend for the proposed tolerance, provided EFB concludes that the crop rotation restriction are appropriate.

DETAILED CONSIDERATIONS

Proposed Uses

Metolachlor, formulated as Dual 8E (8 lb act/gal.), is proposed for preplant or preemergence application for grass and weed control in cotton fields.

Metolachlor alone (Arkansas, Louisiana, Mississippi, New Mexico, Oklahoma, Tennessee, Texas, and Bootheel of Missouri): use a single application at rates of 1.5-2.0 lb act/A depending upon the soil type.

Metolachlor plus prometryne tank-mix: use single application per acre as indicated. 1.25-2.0 lbs metolachlor + 1.2-2.4 lb prometryne per acre in Oklahoma and Blacklands and Gulf Coast of Texas. 1.25-2.0 lb metolachlor + 0.8-1.6 lb prometryne in New Mexico and High Plains, Rolling Plains, Edwards Plateau of Texas and Southwest Texas.

Prometryne, 2,4-bis(isopropylamino)-6-(methylthio)-S-triazine[Caparol], has an established tolerance of 0.25 ppm in cottonseed and 1.0 ppm in cotton forage (§180.222). Prometryne is registered for use on cotton as indicated below.

2.4 lbs (California and Arizona only); preplant application.
Do not graze or feed forage from treated areas to livestock.

2.8 lbs preemergence. Do not use in Arizona and California.

Post emergence applications (2-3) at 0.48-1.6 lbs/A.

Metolachlor plus fluometuron tank-mix: use single applications as indicated. (Arizona, Louisiana, Mississippi, Eastern Oklahoma, Tennessee, Bootheel of Missouri, and Gulf Coast, Rio Grande Valley and Eastern Texas). 1.25-2.0 lbs metolachlor + 1.0-2.0 lbs fluometuron per acre. Treated forage or gin trash is not to be fed to livestock. Do not graze treated areas.

Fluometuron, [1,1-dimethyl-3-(alpha, alpha, alpha-trifluoro-m-tolyl) urea; Cotoran®], has an established tolerance of 0.1 ppm on cottonseed (§180.229). Fluometuron is registered for preemergence applications to soil planted to cotton at 2.0 lb act/A. A maximum of 3 applications is permitted on same crop or field in any year. Post emergence applications are permitted at 1.0 and 2.0 lb act/A. Treated foliage or gin trash is not to be fed to livestock.

The gin trash feeding restriction is not considered practical because the trash is not normally under the control of the cotton farmer after ginning. However, in light of the U.S.D.A. recommendation against the feeding of gin trash (11/4/68), we are not raising any question on the practicality of the restriction or its inclusion on the label.

There are also crop rotation restrictions on the label. We defer to EFB on the appropriateness of these restrictions.

The formulation's inert ingredients are cleared for use under §180.1001. The manufacturing process and the composition of technical metolachlor are discussed in PP8F2081. The impurities are not likely to produce a residue problem.

We have considered the question of the possible presence of nitrosoamines in previous memos (PP#7F1913). We concluded that nitrosoamine formation is unlikely.

Nature of the Residue

We have considered the metabolism of metolachlor in plants and animals in previous reviews (PP#7F1913, 6G1708, 6F1606, 5G1553). Plants (corn, soybeans) absorb, translocate, and metabolize metolachlor. The primary path of plant metabolism involves hydrolysis and conjugation with plant constituents.

Metolachlor is ingested, metabolized, and rapidly eliminated by animals (rats, goats, cattle, chickens) with some deposition of residues in tissues. While the conjugated natural components in animals differ from those in plants, the metabolic components are similar.

The nature of the residue in plants and animals is similar. The significant components of the residues consist of the parent compound and its metabolites: 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol (CGA-37913); and, 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone (CGA-49751). The residue method determines these components and their conjugates.

The nature of the residue is adequately delineated.

Analytical Methods

Metolachlor: a sample is refluxed overnight with dilute hydrochloric acid. (This procedure converts metolachlor, its metabolites, and conjugates to CGA-37913 and CGA-49751). The extract is made basic, and the CGA-37913 is extracted into hexane. This extract is cleaned up on an alumina column followed by a silica gel column and concentrated. The CGA-37913 in the concentrate is determined by gas-liquid chromatography (GLC) using an electrolytic conductivity detector which is sensitive to nitrogen. The results are expressed as ppm metolachlor.

For CGA-49751, the initial sample hydrolysis with dilute hydrochloric acid is as above. The acid extract is partitioned with dichloromethane which separates CGA-49751 and CGA 37913. The dichloromethane phase containing CG-49751 is washed with a dilute sodium carbonate solution, cleaned up on an alumina column, and converted to the chloroethanol derivative by reaction with boron trichloride/2-chloroethanol. The derivative is extracted into hexane, and an aliquot of the extract is cleaned up on a silica gel column followed by an alumina column. The eluate is concentrated, and the CGA 49751 is determined by GLC. The results are expressed as ppm metolachlor.

Untreated (control) samples of cottonseed, hulls, meal, crude oil, refined oil, and soapstock had <0.005-0.05 ppm metolachlor equivalent residues. Control samples were fortified with the metabolites at levels of 0.02-0.2 ppm. Recoveries were 72-106%.

The methods have been successfully tested with metolachlor and its metabolites on corn grain and meat. We believe the results of the method trials can be extended to include cottonseed and its processing fractions.

Adequate analytical methods are available for enforcement purposes.

Prometryne [2,4-bis(isopropylamino)-6-(methylthio)-s-triazine]: two procedures are used to determine residues of prometryne and its metabolites.

Method AG-281 is used to determine metabolite GS-26831, (2,4-diamino-6-methylthio-s-triazine). A sample is extracted by blending with a methanol/water mixture which is washed with hexane and evaporated. The residue is cleaned up by column chromatography and determined by gas chromatography using a nitrogen specific detector.

The parent compound, prometryne, and the metabolite GS-11354, (2-amino-4-isopropylamino-6-methylthio-s-triazine), are determined by method AG-295. A sample is extracted by blending with chloroform. The extract is cleaned up by partitioning between acetonitrile and hexane followed by chromatography of the acetonitrile phase on an alumina column. The components are eluted with ethyl ether in carbon tetrachloride and determined by gas chromatography as above.

Untreated (control) cottonseed samples had <0.10 ppm prometryne-equivalent residues. Control samples, fortified with prometryne and its metabolites at levels of 0.05-1.0 ppm, yielded recoveries of 60-125%.

The method is adequate for the determination of residues of prometryne and its metabolites.

A method suitable for enforcement is included in PAM II. The method has been successfully tested by FDA on cottonseed, cottonseed oil and milk. The method's sensitivity is approximately 0.05 ppm.

Fluometuron, [1,1-dimethyl-3-(alpha, alpha, alpha-trifluoro-m-tolyl) urea]. Samples are examined by method CF-R5 and determined by HPLC. The method determines, as 3-trifluoromethylaniline, total residues of fluometuron, its metabolites, and conjugates that are hydrolyzable to 3-trifluoromethylaniline.

Control samples of cottonseed had <0.05 ppm fluometuron-equivalent residues. Control samples were fortified at levels of 0.05 ppm and 0.40 ppm. Recoveries were 79-94%.

The method is included in PAM II as suitable for enforcement purposes for fluometuron. (The 3-trifluoromethylaniline is determined colorimetrically; however, the extraction procedure is essentially the same.)

Adequate analytical methods are available for enforcement purposes.

Residue Data

Samples were obtained from crops in Arkansas, Louisiana, Mississippi, Texas, and New Mexico which had been treated with metolachlor alone or in tank-mix combinations with prometryne or fluometuron. The crops were sampled at 149-199 days after treatment (PHI).

Cottonseed had no detectable residues (<0.05 ppm, analytical sensitivity) of metolachlor or its metabolites due to metolachlor treatment alone at 1X and 2X the maximum proposed rate or in tank-mix combinations at the maximum proposed rate.

No residues of prometryne (<0.10 ppm) or fluometuron (<0.05 ppm) were noted in cottonseed due to the maximum proposed rates. Thus, residues of prometryne or fluometuron in or on cottonseed are not likely to exceed the established tolerances for prometryne (0.25 ppm) or fluometuron (0.1 ppm).

Cottonseed byproducts:

Cottonseed which contained maximum metolachlor residues of 0.019 ppm (as determined by a combination of gas chromatography and mass spectrometry, GC-MS) were processed, and the fractions were analyzed for metolachlor residues by the chemical method (sensitivity of about 0.05 ppm).

No residues were detected in the hulls, meal, oil, or soapstock.

Residues of metolachlor and its metabolites in or on cottonseed or its byproducts (hulls, meal, oil, soapstock) are not likely to exceed the proposed tolerance (0.1 ppm).

Meat, Milk, and Eggs

Cottonseed and cottonseed hulls, meal, and soapstock are occasionally used as livestock feeds. The maximum level of metolachlor residues likely to be ingested by livestock can be estimated through the use of the percentages of each item in the diet and the proposed tolerance of 0.1 ppm.

The maximum ingestion levels are: cattle (0.013 ppm); sheep and goats (0.010 ppm); horses (0.008 ppm); and, hogs and poultry (0.005 ppm).

Permanent tolerances are established at 0.02 ppm in eggs, milk, meat, fat, and meat byproducts of livestock (§180.368). These tolerances are supported by livestock feeding studies in which dairy cows and goats were fed metolachlor residues at levels of 0-5 ppm and laying hens were fed at levels of 0-2 ppm (PP#s 7F1913, 9F2203, 9F2213). In view of the ingestion levels indicated above, we conclude that any metolachlor residues which might occur in eggs, milk, or meat due to the feed use of cottonseed and its byproducts (hulls, meal, soapstock) would be adequately covered by the established tolerances [§180.6(a)(2)].

TS-769:RCB:A. Smith:gs:X77377:RM810:CM#2:7/2/81
cc: RF, Circ.(3), A. Smith, Watts, FDA, TOX, EEB, EFB, PP#1F2506
RDI: Quick, 6/26/81

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Metolachlor

PETITION NO. 1F2506

CCPR NO. None

Codex Status

☒ No Codex Proposal
Step 6 or above

Residue (if Step 9): _____

Crop(s) Limit (mg/kg)

None

Proposed U.S. Tolerances

2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide and its metabolites 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol and 4-(2-ethyl-Residue: 6-methylphenyl)-2-hydroxy-5-

methyl-3-morpholinone

Crop(s) Tol. (ppm)

Cottonseed 0.1

CANADIAN LIMIT

Residue: _____

Crop Limit (ppm)

None (on cottonseed)

MEXICAN TOLERANCIA

Residue: _____

Crop Tolerancia (ppm)

None

NOTES: