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

FEB 22 1982

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP# 1E2563. Metolachlor in Rotational Grain Crop Forage and Fodder. Evaluation of Analytical Methodology and Residue Data.

EPA Reg. No. 100-597. Request for Amended Registration of Dual® 8E Herbicide to Permit the Forage and Fodder from Rotational Grain Crops to be Used for Livestock Feed.

FROM: M. Nelson, Chemist mjn
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THRU: Charles L. Trichilo, Chief
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TO: Richard Mountfort, Product Manager #23
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Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

The Ciba-Geigy Corporation proposes tolerances for combined residues of the herbicide metolachlor [2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide; trade name, Dual®; aka CGA-24705] and its metabolites determined as 2-[(2-ethyl-6-methylphenyl)-amino]-1-propanol [aka CGA-37913] and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone [aka CGA-49751], each expressed as parent metolachlor, in the raw agricultural commodity rotational grain crop forage and fodder at 0.5 ppm.

The petitioner also requests amended registration of the Dual® 8E herbicide label (EPA Reg. No. 100-597) to permit the forage and fodder of rotational grain crops to be fed to livestock.

Tolerances are presently established (40 CFR 180.368) for aforesaid combined residues from purposeful usage in or on field corn, peanuts, soybeans, and sorghum at levels ranging between 0.1-3 ppm. There are also tolerances established for secondary residues in meat, milk, poultry, and eggs at 0.02 ppm.

Additional tolerances are co-pending on sweet corn, popcorn, safflowers, sunflowers, flax, cottonseed, potatoes, and seed and pod vegetables at levels ranging between 0.1-1 ppm. These also are a result of target crop usage.

The proposed tolerance(s) of this present petition, if and when established, will be for aforesaid combined residues in the specified rotational crops, where the residues in said crops result from the uptake of the carryover in soil of these pesticide residues from treatment of previous crops. [See 46 FR 3018, 1/13/81, General Statement of EPA Policy re Tolerance Setting for Pesticide Residues in Rotational and Follow-Up Crops, Meat, Milk, Poultry, and Eggs, and for Other Indirect or Inadvertent Residues under Sec. 408(e) of the Federal Food, Drug, and Cosmetic Act.]

Clarification has been obtained from the petitioner (telecon of 1/12/82, R. Quick, RCB and G. Holt, Ciba-Geigy) that, by the terminology "rotational grain crop forage and fodder", the petitioner is actually referring to the forage and fodder of grain crops as defined in 40 CFR 180.34(f). This encompasses "any crop belonging to the family Graminae that produces mature seed that are used for food or feed, barley, buckwheat, corn (field corn, sweet corn, and popcorn), millet, milo, oats, rice, rye, sorghums (grain), wheat."

Said telecon also clarified that the grains per se of these rotational crop forages and fodders were intentionally not included in the tolerance proposed because no detectable residues were reported in the grains per se in the "cold" (unlabeled) field residue studies. [Low level (below the sensitivity of the enforcement methodology) residues of total ^{14}C, expressed as ppm metolachlor, were reported in the grains per se in the tracer studies with rotational crops; see Nature of the Residue.] The petitioner's representative indicated, however, that the Company would not object to proposing a suitable tolerance for the rotational grains per se should our review deem it appropriate.

Conclusions

1. The nature of the residue in plants and animals is adequately delineated. The residue of concern is parent metolachlor and its metabolites determined as CGA-37913 and CGA-49751.

2. Adequate analytical methodology is available for enforcement purposes.

3a. Residues in rotational grain crop forages and fodders are not expected to exceed the proposed 0.5 ppm tolerance.

3b. A tolerance (0.1 ppm) should be proposed for the grains of the rotational grain crops.

3c. Section F needs to be revised to individually list each rotational grain crop grain and its corresponding forage and fodder for which tolerances are sought.

4. The existing meat/milk/egg tolerances are adequate to cover residues arising from both the registered uses and those proposed herein.

5. The amended registration request to revise the Dual® 8E herbicide label to permit the forage and fodder (and grains, if desired) of rotational grain crops to be fed to livestock is supportable.

6. An International Residue Limit (IRL) Status sheet is attached. There is no IRL established for metolachlor which is applicable to its residues in rotational crops.

Recommendations

Contingent upon favorable resolution of the deficiencies stated in Conclusions 3b and 3c, and TOX and EFB considerations permitting, we can recommend in favor of the establishment of tolerances for the combined residues of metolachlor and its metabolites determined as CGA-37913 and CGA-49751 in the various (to-be-specified) grains (at 0.1 ppm), forages and fodders (at 0.5 ppm) of rotational grain crops.

With the same caveats, we also recommend favorably for the amended registration request to revise the Dual® 8E herbicide label to permit the forage and fodder (and grains, if desired) of rotational grain crops to be fed to livestock.

Notes to P.M.: (1) These rotational crop tolerances, if and when established, will need to be distinguished in the Regulations from other pesticide tolerances which imply a registered (target crop) use. [Ref. Rotational Crop Policy Statement, 46 FR 3018ff, 1/13/81.]

(2) Dual® 8E may be tank-mixed with a number of different pesticides (see label). The possibility that residues of those tank-mates and/or their metabolites may also occur at detectable levels in rotational crops (specifically, in this case, in rotational grain crop forages and fodders, and perhaps in the grains per se as well) can not presently be ruled out.

In fact, there is some field trial data for Dual 8E + AAtrex combinations [see AG-A 5473, 5513, and 5558 on pp. 134, 143, and 154, Sec. D (Vol. II), this petition] which shows that low level detectable residues of the tank-mate can indeed result in the forage and fodder at least of a rotational grain crop.

RCB defers to the P.M. to initiate whatever administrative action (if any) is considered necessary on the Agency's part to assure tolerance regulation of tank-mate residues in rotational crops in this eventuality.

Detailed Considerations

Manufacture and Formulation

The manufacturing process and the composition of technical metolachlor are detailed in our (A. Smith) 4/2/79 review of PP# 8F2081, which see.

The technical product is a minimum of 90% pure; the remaining ca 10% is composed of various reaction by-products and impurities, none of which is expected to cause a residue problem.

The question of the possible presence of nitrosamines has been considered previously (see PP# 7F1913) and discounted as unlikely (ref. 9/6/78 review of D. Reed and W. Boodee).

Technical metolachlor is the active ingredient in Dual® 8E Herbicide (EPA Reg. No. 100-597), an emulsifiable concentrate formulation containing 8 lbs ai/gal. It is this formulation which is to be utilized for the proposed uses under consideration herein.

Inert Ingredient Information Deleted

A Confidential Statement of Formula for Dual® 8E is contained within Section A of this petition. The composition of the formulation is identified as being comprised of technical metolachlor as the a.i. [redacted] indicated as being cleared for use under 40 CFR 180.1001 (c) or (d).

The percentage-by-weight composition for this formulation which is listed on the Dual® 8E label is 86.4% ai and 13.6% inerts. This takes into account the purity of the ai resulting from the manufacture of the technical product, which is claimed to be typically 95-97%.

Proposed Use

Dual® 8E is a selective herbicide currently registered as a preplant incorporated or preemergence surface-applied treatment in water or fluid fertilizer for control of most annual grasses and certain broadleaf weeds in the target crops field corn, soybeans, peanuts, grain sorghum, and woody ornamentals.

Dual® 8E is applied by ground rig or aircraft at rates up to 3 lbs ai/A (i.e., 3 pts of formulation) alone, or in tank mixtures with labeled rates of AAtrex, Amiben, Banvel, Bladex, Dyanap, Lexone, Lorox, Milogard, Princep, Sencor, Paraquat CL, Roundup, or Igran.

The current Dual® 8E labeling re rotational crops states that: 1) If crop treated with Dual® 8E alone is lost, corn, soybeans, peanuts, or Concep®-treated grain sorghum may be replanted immediately. Do not make a second broadcast application of Dual® 8E. If the original application was banded and the second crop is planted in the untreated row middles, a second banded treatment may be applied. 2) Barley, oats, rye, or wheat may be planted 4-1/2 months following treatment. Grain crops, cotton, soybeans, peanuts, and root crops may be planted in the spring following treatment. Do not graze or feed forage or fodder from cotton or small grains to livestock. 3) All other rotational crops may be planted 18 months after application.

Note: If/when Dual® 8E is tank-mixed with another pesticide (see listing above), the label instructions re rotational crops for each individual product involved must be taken into consideration, and the most conservative followed.

The purpose of this present petition is to support the establishment of the proposed tolerance in the forage and fodder of rotational grain crops, thereby allowing the removal from the Dual® 8E label of the current grazing restriction thereof.

An application to amend Dual® 8E registration (EPA Reg. No. 100-597) to permit the use of forage and fodder from rotational grain crops for livestock feed has been submitted simultaneously with this petition. This request will also be considered within the scope of this present review.

Nature of the Residue

Radiotracer (^{14}C) metabolism data are available from metolachlor studies on corn, soybeans, lettuce, and potatoes treated as target crops and carrots, soybeans, winter wheat, and oats grown as rotational crops in previously treated soils.

Plants absorb, translocate, and metabolize metolachlor. The primary path of plant metabolism in target crops involves hydrolysis and conjugation with plant constituents. The metabolites in rotational crops are believed to be the same as those in target crops.

The significant components of the residue in plants consist of parent metolachlor and its metabolites determined as 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol and 4-(2-ethyl-6-methylphenyl)

-2-hydroxy-5-methyl-3-morpholinone. The analytical methodology used for enforcement purposes determines these components and their conjugates.

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

Radiotracer (^{14}C) metabolism data are also available from metolachlor studies with rats and lactating goats, and feeding study data is available from dairy cattle and poultry.

Metolachlor is ingested, rapidly metabolized, and almost totally eliminated by animals; there is only minor deposition of residues in tissues, milk, and eggs. While the conjugating natural components in animals differ from those in plants, the aglycone metabolic components are similar. The significant components of the residue in animals are thus the same as those in plants.

We consider the nature of the residue in animals to be sufficiently delineated.

* * *

Since the ^{14}C metabolism studies on the rotational grains (winter wheat and oats) are of particular relevance in our considerations of the proposed tolerance(s), and since these studies have not previously been submitted, they are discussed in some detail below.

A greenhouse study was conducted to determine the uptake of ^{14}C-metolachlor and its aged soil degradation products in rotational winter wheat (GAAC-74071) and rotational oats (GAAC-74085). Winter wheat was grown in silt loam soil treated with 2 lbs. ai/A ring-labeled ^{14}C-metolachlor six months earlier. To simulate field conditions, winter wheat was allowed to grow on a short day schedule for thirty days and then vernalized in cool temperatures for one month. After vernalization, normal temperatures were resumed and the plants grown to maturity. Plant analyses were conducted immediately prior to vernalization and five, ten, and fifteen weeks after the beginning of spring growth. Rotational oats were grown in silt loam soil treated with 2 lbs. ai/A ring-labeled ^{14}C-metolachlor nine months earlier. Plants were analyzed four, eight, and fourteen weeks after germination. Soils were analyzed at specific intervals.

Results indicate total ^{14}C-radioactivity in the 0-9 inch soil layer remained approximately constant (1 ppm) during the growth of rotational crops. At planting, approximately 80% of the total ^{14}C-radioactivity was nonextractable. At plant maturity, the 0-3 inch soil layer contained 0.60 ppm (winter wheat) and 0.55 ppm (oats) equivalent to ^{14}C-metolachlor. Approximately 83% of the total ^{14}C-residue in each soil was not extractable. As was observed in the

^{14}C-labeled field rotational studies, soil data suggest an equilibrium between extractable and nonextractable ^{14}C-metolachlor residues was reached before the growth of rotational crops and was maintained during the growing period. This equilibrium may provide soluble ^{14}C-residues for plant uptake, soil leaching, or further degradation. Leaching of ^{14}C-residues from the 0-3 to 3-6 inch soil layer was observed during this study.

Based on total ^{14}C- radioactivity, winter wheat contained 0.14 ppm equivalent to ^{14}C-metolachlor prior to vernalization. This concentration remained constant until maturity when desiccation resulted in an increase in winter wheat straw to 0.60 ppm. The grain contained 0.03 ppm equivalent to ^{14}C-metolachlor; most (62%) of the ^{14}C-residues were extractable, aqueous-soluble materials. The solubility and ionic character of the plant metabolites were similar to those present in the target crop, corn.

Rotational oats grown under greenhouse conditions contained 0.17 ppm equivalent to ^{14}C-metolachlor at the four-week harvest. This concentration remained approximately constant until maturity when desiccation of the plants resulted in an increase in oat straw to 0.27 ppm equivalent to ^{14}C-CGA-24705. The grain contained 0.05 ppm equivalent to ^{14}C-CGA-24705. Approximately 67% of the radioactivity in mature oat straw was aqueous soluble and 22% was non-extractable. The solubility and ionic character of the plant metabolites were similar to those present in the target crop, corn.

In summary, ^{14}C-metolachlor studies have shown that residues are not present in significant quantities in rotational wheat or oat grain. Measurable residues are present in the at-harvest straw samples of wheat and oats, primarily due to the desiccation process and the fact that they were conducted under greenhouse conditions which tend to produce higher residue levels than under normal field conditions. The following table summarizes these results:

Total ^{14}C-Residues in Rotational Crops
Equivalent to ^{14}C-Metolachlor

Crop and Portion		^{14}C-Residues (ppm)
Winter Wheat	Straw	0.60
	Grain	0.03
Oats	Straw	0.27
	Grain	0.05

Comparison of solubility and ionic characteristics with previous studies indicate the metabolites in rotational wheat and oats are probably the same as those in the target crop, corn.

Analytical Methodology

Four different versions (AG-265, AG-277, AG-286, and AG-338) of the basic analytical method were utilized over the years in analyzing various of the field trial residue data submitted in support of this petition.

Metolachlor residues in the grain, forage, and fodder of winter wheat and oats planted as rotational crops were determined initially by employing the analytical method described in AG-265. By this method, the majority of residues are hydrolyzed to a single moiety, 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol (CGA-37913) by refluxing overnight in hydrochloric acid. After basification, the CGA-37913 residues are partitioned from the aqueous extract into hexane. The hexane is passed through an activated aluminum oxide clean-up column to remove compounds which interfere with the quantitation of the CGA-37913 residues which are determined using a nitrogen-specific gas chromatographic system.

It was found later that additional residues could be determined after acid hydrolysis as 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone (CGA-49751). The procedures for determining this compound plus CGA-37913 are described in AG-277. AG-277 is a modification of AG-265 which includes partitioning, clean-up,derivatization, and determination by microcoulometric GLC.

A modified version of AG-277 is described in AG-286, which is the regulatory method in PAM II, and the method which has previously undergone successful method trial (in re PP# 5F1606) in our laboratories.

AG-338 is an updated version of the regulatory method and utilizes separate aliquots for the determination of CGA-37913 and CGA-49751. The more recent field trial data were analyzed by this procedure.

Details of this latest version (AG-338) are as follows:

Metolachlor residues are converted to CGA-37913 and CGA-49751 by refluxing with 6N hydrochloric acid overnight. CGA-37913 is determined as follows: An aliquot for the acid extract is basified with 50% (w/w) sodium hydroxide (19.4N) and CGA-37913 is partitioned into hexane. This fraction is subsequently chromatographed on an alumina clean-up column to remove interfering compounds. Final determination is performed on a gas chromatograph equipped with a Hall electrolytic conductivity detector specific for nitrogen or an alkali flame ionization (N-P) detector operating in the nitrogen-specific mode. The CGA-37913 residues are reported as metolachlor equivalents. The limit of detection is 0.03 ppm.

For CGA-49751: An aliquot of the acid extract is partitioned with dichloromethane to extract CGA-49751 into the non-aqueous phase. The dichloromethane-containing CGA-49751 is partitioned with a 5% sodium carbonate solution and chromatographed on an alumina column to remove interfering materials. CGA-49751 is converted to the chloroethanol derivative by reaction with boron trichloride/2-chloroethanol at 90°C for 15 minutes. The products are partitioned with hexane and chromatographed on a silica gel column followed by an alumina column. Final determination is performed on a gas chromatograph equipped with an alkali flame ionization (N-P) detector operating in the nitrogen-specific mode. The CGA-49751 residues are reported as metolachlor equivalents. The limit of detection is 0.05 ppm.

Validation data showing recoveries of CGA-37913 and CGA-49751 from the various substrates (grain, forage, fodder) are submitted for these differing versions of the basic analytical method. Adequate recoveries and low control values were consistently reported.

We conclude that adequate analytical methodology is available to support the proposed tolerance(s).

Note: Regulatory methodology is available in PAM II for the tank-mates which may be used with Dual® 8E.

Residue Data

Winter wheat was grown as a rotational crop following metolachlor applications to corn or soybeans. Studies were conducted in 1973, 1976, 1977, and 1978. Rates of metolachlor ranged from 2.0 to 4.0 lbs. ai/A. Metolachlor was applied alone as 250EC, 6E, 8E, or in tank mixture with atrazine.

A total of 13 tests were conducted in eight states (MS, NE, IL, MD, PA, AL, CA, WI) to provide adequate geographic distribution. The wheat was planted 3 to 7 months following the initial application. Samples of forage, fodder (straw, stover), and grain were taken for analysis.

The maximum residues found were:

Number of Tests	Wheat Substrate	Maximum Residue (ppm) Metolachlor Rate (lbs. ai/A)			
		2.0	2.5	3.0	4.0
10	Forage (fall or spring)	<0.08	0.05	0.09	0.11
13	Fodder (straw, stover)	0.13	0.20	0.32	0.32
12	Grain	<0.08	0.05*	<0.08	<0.08

*Corresponding control sample contained apparent metolachlor residue.

Residues are "Total" residues determined as CGA-37913 and CGA-49751 and expressed as metolachlor equivalents.

Results are in agreement with previously submitted ^{14}C work. No grain residues were found (<0.08 ppm) except where a gas chromatographic interference peak was also noted in corresponding control samples.

Forage and fodder (stover, straw) residues are dose dependent and reflect the dehydration/desiccation enhancement at harvest time.

Oats were planted as a rotational crop following metolachlor 250EC applications to corn in 1973. Three tests were conducted in three states (MS, NE, IL) with the oats being planted 4 to 12 months following the initial application.

Application rates range from 2 to 4 lbs. ai/A. Samples of forage, straw (stover), and grain were taken for analysis.

The maximum residues found were:

Number of Tests	Oat Substrate	Maximum Residue (ppm) Metolachlor Rate (lbs. ai/A)	
		2.0	4.0
2	Forage	0.04	0.05
3	Fodder	<0.08	<0.08
2	Grain	<0.08	<0.08

Residues are "Total" residues determined as CGA-37913 and CGA-49751 and expressed as metolachlor equivalents.

Again, no residues were found in harvest grain (<0.08 ppm) and only minimal residues were found in forage samples. Fodder samples contained no detectable residues.

<u>Comments.</u> Radiolabeled studies (see Nature of the Residue Section) have shown accumulations of ^{14}C-metolachlor in the forage amd fodder of rotational winter wheat and oats up to 0.60 ppm equivalent to metolachlor. Field studies conducted across the United States on rotational winter wheat and oats show a maximum residue of 0.32 ppm as determined by enforcement methodology.

Based on the agreement of these radiolabeled and non-radiolabeled rotational studies, plus what is known about the uptake of metolachlor in target crops, the results support the establishment of a tolerance in rotational grain crops forage and fodder (straw, stover) of 0.5 ppm.

Section F will need to be revised to specifically list the individual grain crop forages and fodders which are to be involved. The proposed tolerance for rotational grain crop forages and fodders can not be established on a crop grouping basis since a non-negligible level (0.5 ppm) is involved.

Additionally, we request that a low level tolerance be proposed for the corresponding rotational grain crop grains per se, even though no detectable residues in rotational grains per se were reported in the "cold" field studies.

We consider this an advisable regulatory safeguard since low levels of residues (0.03-0.05 ppm equivalent to metolachlor) were reported in the grains per se in the ^{14}C rotational winter wheat and oats studies submitted (see Nature of the Residue Section).

We suggest 0.1 ppm as a suitable level [reflects combined method sensitivities of CGA-37913 (0.03 ppm) plus CGA-49751 (0.05 ppm), rounded upward] for a tolerance proposal for the grains per se of rotational grain crops. A revised Section F reflecting this should be submitted.

For clarity, we request the rotational grains per se be individually listed in Section F; the listing of which individual rotational grains per se the to-be-proposed 0.1 ppm tolerance is to cover should be consistent with the listing of the individual rotational grain forages and fodders which the proposed 0.5 ppm tolerance is to cover.

As for the possibility of detectable residues arising in rotational grain crop forage, fodder and/or grain per se from the pesticides which may be applied in tank-mix combination with Dual® 8E, please see Notes to PM., No. 2, Recommendations Section.

[Note: We gave some consideration as to whether rice should be excluded from any favorable recommendation we might make herein re the establishment of proposed tolerances for the forages and fodders (and grains) of rotational grain crops.

We based this on: (1) the disparity in cultural practice between rice and other grain crops, and (2) the absence of actual field trial residue data from rice grown as a rotational crop.

It was our conclusion, however, that it was not necessary to exclude rice from the "rotational grain crop forage and fodder" proposed tolerance requests.

We predicated this on: (1) previously submitted soil data showing the half-life of metolachlor in soil to be 1-2 months. Since the earliest a rotational crop can be planted is approximately 4-1/2 months (per the Dual® 8E label restrictions) after an initial application to corn or similar target crop, less than 25% of the metolachlor remains available to the rotational crop for uptake. This reults in a substantially lower residue in the forage, fodder, and grain of rotational grain crops as compared with target grain crops. It is therefore not reasonable to presume that rice would exhibit a markedly enhanced residue picture as compared to other rotational grain crops, and (2) rice forage and fodder (straw) is only a very minor livetock feed item (see Harris Guide) and it would not be economically feasible for livestock to be fed rice grain in significant quantities on a routine basis.]

Residues in Meat, Milk, Poultry, and Eggs

Tolerances of 0.02 ppm are presently established (40 CFR 180.368) for combined residues of metolachlor and two of its metabolites in eggs, milk, and the meat, fat, and meat by-products of cattle, goats, hogs, horses, poultry, and sheep from registered uses of metolachlor formulations on various crops.

The tolerance proposals and amended registration associated with this present petition will not affect the adequacy of those established milk/egg/meat tolerances; i.e., the present egg/milk/meat tolerances are adequate to cover residues arising from both the presently registered and herein proposed usages. [Note: Cattle, goats, and chicken feeding studies were submitted in re PP# 7F1913, which see for details.]

We therefore can also conclude that the amended registration request to revise the Dual® 8E herbicide label to permit the forage and fodder (and grains) of rotational grain crops to be fed to livestock is supportable.

Other Considerations

An International Residue Limit (IRL) Status Sheet for metolachlor is attached to this review. There is no IRL established for metolachlor which is applicable to its residues in rotational crops.

Attachment

TS-769:RCB:Reviewer:M.Nelson:EFB:LDT:CM#2:RM:810:Date:2/12/82
cc: RF., Circ, Nelson, Thompson, FDA, TOX, EEB, EFB, PP# No. 1E2563
RDI: Quick: 1/21/82; Schmitt, 1/22/82

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Metolachlor

Petition NO 1E2563

CCPR NO. None

Codex Status

/X/ No Codex Proposal
Step 6 or above

Residue (if Step 9): ________

Crop(s)	Limit (mg/kg)
none	

Proposed U. S. Tolerances

for 180.368

Residue: metolachlor plus two metabolites

Crop(s)	Tol. (ppm)
rotational grain crop forage and fodder	0.5

CANADIAN LIMIT

Residue:

metolachlor

Crop	Limit (ppm)
corn	0.1 1/

MEXICAN TOLERANCIA

Residue: ________

Crop	Tolerancia (ppm)
none	

Notes: 1/ Negligible residue type tolerance