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

CONFIDENTIAL

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

AUG 7 1990

MEMORANDUM:

SUBJECT: New Chemical Review: PP#9F3755/9H5583: Quinclorac (FACET) in or on Rice Grain and Straw. Evaluation of Analytical Method and Residue Data. MRID Nos. 410635-01 through 03, 410635-34 through -46, 410761-01 and 410761-04. FFDCA Sections A through G. No MRID No. DEB No. 5554.

FROM: Joel Garbus, PhD., Chemist
Permanent Tolerance Section III
Dietary Exposure Branch (H7509C)

THROUGH: Richard D. Schmitt, PhD., Chief
Dietary Exposure Branch
Health Effects Division (H7509C)

TO: R. Taylor / J. Miller PM-25
Registration Division (H7505C)

BASF Corporation Chemical Division, Parsippany, NJ has petitioned for the following permanent tolerances for its herbicide 3,7-dichloro-8-quinoline carboxylic acid [quinclorac, FACET, BAS 514H]:

Rice grain		5.0 ppm
Rice straw		12.0 ppm
Cattle	fat, meat, and MBYP	0.05 ppm
Goat	fat, meat, and MBYP	0.05 ppm
Hogs	fat, meat, and MBYP	0.05 ppm
Horse	fat, meat, and MBYP	0.05 ppm
Sheep	fat, meat, and MBYP	0.05 ppm
Poultry	fat and meat	0.05 ppm
Poultry	MBYP	0.10 ppm
Milk		0.05 ppm
Eggs		0.05 ppm

and for the following feed/food tolerance:

Rice bran	15.0 ppm

This is the first food use for this chemical.

Summary of Deficiencies

- The petitioner should provide evidence that the name quinclorac has been accepted by ANSI. In the absence of such acceptance the chemical name 3,7-dichloro-8-quinoline-carboxylic acid is suitable for use.

- A reference sample suitable for enforcement analytical methodology purposes is needed for the EPA Repository.

- The petitioner must explain and resolve the discrepancies between the analyses of production batches and the list of impurities and their levels given on the CSF.

- An explanation is needed for the process of arriving at certified limits.

- The petitioner needs to provide a revised CSF based upon the analyses of actual production lots.

- A label restriction is needed regarding the use of treated rice fields for aquaculture. Alternatively, the petitioner can determine residues in catfish and crayfish raised in treated fields and propose tolerances for these commodities if necessary.

- In rice processing studies, fractions were stored for 13 months prior to analysis The length of the storage time in the submitted storage stability studies was eight months. The petitioner needs to submit additional data as to the stability of quinclorac residues in stored rice processing fractions.

Conclusions

1. With the exceptions noted below the product chemistry requirements for quinclorac have been met.

1a. The petitioner should provide evidence that the name quinclorac has been accepted by ANSI. In the absence of its acceptance by ANSI the chemical name 3,7-dichloro-8-quinoline-carboxylic acid is suitable for use as the rubric for tolerances, for the descriptive contents portion of the label, and for the CSF.

1b. The provision of sample suitable for enforcement analytical methodology purposes is a requirement of the product chemistry and residue chemistry sections of 40 CFR 158. The petitioner will need to provide a sample of quinclorac to the EPA repository and inform the Agency that this has been done.

1c. There are discrepancies between the impurities identified in the analyses of pre-production batches and those listed on the CSF.

Impurities listed as occurring in amounts greater than 0.1% are not listed on the CSF. Conversely impurities given as present at less than 0.1% are listed on the CSF. Impurities that, from the results of batch analyses, should be listed on the CSF are not so listed and components are listed on the CSF that are not reported in the batch analyses. The petitioner must explain and resolve these discrepancies.

1d. No explanation is proffered for the process of arriving at certified limits. A description of the manner of determining the certified limits is needed.

1e. The petitioner needs to provide a revised CSF based upon the analyses of actual production lots.

2. The plant and animal metabolism studies are satisfactory and demonstrate that the residue of regulatory concern in plants and animals is quinclorac, per se.

3a. For postemergence applications, FACET is to be applied with the addition of a spray adjuvant, BCH 864 01 S, that is used to improve the consistency of weed control. The PM should ascertain that the ingredients of the adjuvant, a detergent and a solvent, are cleared inerts.

3b. The use directions are satisfactory provided a restriction against aquaculture is added to the label. Such a restriction is needed if the petitioner does not present residue data for catfish and crayfish. Alternatively the petitioner can determine residues in catfish and crayfish raised in treated fields and propose tolerances for these commodities if needed.

4. The proposed analytical methodology has been validated and is suitable for enforcement purposes.

5. Storage stability and accountability has been demonstrated for the proposed analytical procedures for all studies except the rice processing study.

6. It was demonstrated that the multi-residue protocols do not determine quinclorac.

7. The proposed tolerances for rice straw and grain are supported by the results of the residue trials. The residue trials included all of the major domestic rice growing areas and were conducted in a satisfactory manner.

8. The proposed food/feed additive tolerance for rice bran is supported by the results of the rice processing study, provided that the results of the requested study of storage stability of rice processing fractions is satisfactory. The processing and analytical portions were conducted in a satisfactory manner.

9. The proposed meat, milk, poultry, and egg tolerances are supported by the results of feeding studies. This studies were satisfactorily conducted.

10. There are no Codex, Canadian, or Mexican tolerances for quinclorac.

Recommendation

DEB recommends against the granting of the tolerances proposed in this petition because of the deficiencies cited in conclusions 1a, 1b, 1c, 1d, 1e, 3a, 3b, 5, and 8.

PRODUCT CHEMISTRY

BASF had submitted limited product chemistry data in conjunction with its request for an EUP for quinclorac. (See EUP No.7969-EUP-E1, reviewed by S. Hummel, 2/26/88) These data are resubmitted with the current petition.

Product Chemistry Data Requirements (40 CFR 180.120)

61-1: Product Identity and Disclosure of Ingredients

The registrant is required to provide the name, nominal concentration and certified limits and the name, nominal concentration and upper limit of each impurity. For each active ingredient the information should include the molecular, empirical, or structural formulas; the CA name, the CAS number; and the molecular weight.

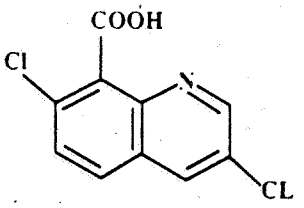
Chemical Name

3,7-dichloro-8-quinolinecarboxylic acid

Common Name

quinclorac (proposed)

Structural Formula:



Empirical Formula: $C_{10}H_5Cl_2NO_2$

Molecular Weight: 242.1

CAS Registry Number: 84087-01-4

Confidential Statement of Formulation:

BASF has supplied a revised Confidential Statement of Formulation for technical quinclorac based upon a more highly purified product resulting from changes in manufacturing procedures. (See Confidential Appendix)

Comment:

There is no accepted common name for 3,7-dichloro-8-quinolinecarboxylic acid. To our knowledge the proposed common name, quinclorac, has not been accepted by the American National Standards Institute (ANSI).

The petitioner should provide evidence that the name quinclorac has been accepted by ANSI. In the absence of its acceptance by ANSI the chemical name 3,7-dichloro-8-quinolinecarboxylic acid should be used as the

rubric for tolerances, for the descriptive contents portion of the label, and for the CSF.

61-2: Description of the Beginning Materials and Manufacturing Process

61-2: Discussion of the Formation of Impurities

The guidelines require that the suppliers of beginning materials be identified and that full descriptions of the manufacturing process be provided. The descriptions of the manufacturing process should include a discussion of each individual reaction in the process, the relative amounts of the reacting materials, the physical conditions of each step, and any purification procedures.

A discussion is required to account for the presence of potential or actual impurities based upon knowledge of the composition of beginning materials, desired and side reactions of the manufacturing process, and contamination or degradation of the active material.

The data that the registrant has submitted in response to this requirement is given and discussed in the Confidential Appendix.

62-1: Preliminary Analysis

62-2 Certification of Limits

62-3 Analytical Methods to Verify Certified Limits

Five or more samples, representative of different manufactured batches, should be analyzed by appropriate methods for active ingredients and for each impurity with results given for each sample. The analytical methods should be referenced to well-known, accepted procedures or a complete description should be given including validation of precision and accuracy.

A certification of upper and lower limits of the active ingredient and upper limits for each impurity is required. The values for the limits should be based upon a consideration of the values for the actual levels of active ingredients and impurities as shown by the analyses of the samples. An explanation is required of the procedures used to establish the certified limits.

The data that the registrant has submitted in response to these requirements is presented and discussed in the Confidential Appendix.

63-2 through 63-21: Physical and Chemical Characteristics

Methods used to meet the requirements of sections 63-2 through 63-21 shall be referenced or described in the application for registration. Only the physical and chemical characteristics of the technical grade material will be considered.

CHARACTERISTIC	VALUE	METHOD
63-2: Color	TGAI: White/Yellow PAI: White	Not Given
63-3: Physical State	Solid	Not Given
63-4: Odor	Practically odorless	Not Given
63-5: Melting Point	TGAI: 269° C PAI: 237° C	Not Given
63-6: Boiling Point	Not Applicable	
63-7: Density	500g/l loose. 630g/l compacted 560g/l	WHO Method WHO Method BASF Method
63-8: Solubility	Water: 0.0064 g/100 ml Ethanol: 0.2 g/100 ml Acetone: 0.2 g/100 ml Toluene: <0.1 g/100 ml n-Hexane: <0.1 g/100 ml Ethyl Acetate: 0.1 g/100 ml Lutrol: <0.1 g/100 ml N-octanol: <0.1 g/100 ml Olive oil <0.1 g/100 ml Acetonitrile: <0.1 g/100 ml 1,2-propandiol: <0.1 g/100 ml Ethyl acetate: 0.1 g/100 ml Dichloromethane: <0.1 g/100 ml Ethyl ether: 0.1 g/100 ml	
63-9: Vapor Pressure	Not Applicable as material is solid at room temperature. The vapor pressure is given as 10^{-7} mbar at 20°C.	
63-10: Dissociation Constant	pK_a 4.34 @ 20°C 4.35 @ 25°C	BASF 88/0137
63-11: Partition Coefficient	0.047 to 0.485 depending upon pH (See MRID 405732-01)	
63-12: pH	3.8 @ 20°C of saturated solution	BASF 89/0059

CHARACTERISTIC	VALUE	METHOD
63-13: Stability	No significant decrease over 2 years at 20,30, and 40°C (See MRID 403208-03)	
	No degradation after 2 weeks at 54°C	CIPAC MT 46
63-14: Oxidizing/Reducing Activity	No oxidizing Activity. Slight reducing activity in presence of strong oxidant.	
63-15: Flammability	Not applicable	
63-16: Explodability	Does not present an explosion hazard.	
63-17: Storage Stability	Stable for two years	
63-18: Viscosity	Not applicable	
63-19: Miscibility	Not applicable	
63-20: Corrosiveness	As an acid quinclorac is corrosive to metals.	
63-21: Dielectric Breakdown Voltage	Not applicable	
64-1: Submission of reference sample	Petitioner will supply samples upon request	

Comment:

The petitioner has adequately met the requirements for sections 63-2 through 63-21 regarding the physical/chemical characteristics of technical quinclorac.

The provision of sample suitable for enforcement analytical methodology purposes is a requirement of the product chemistry section for registration. The petitioner will need to provide a sample of quinclorac to the EPA repository and inform the Agency that this has been done.

RESIDUE CHEMISTRY

Proposed Use

Quinclorac is labeled for weed control in rice. The formulated product (FACET) contains 50% quinclorac as active ingredient and 50% inert ingredients. Clearance of all inerts is within the purview of the Registration Division.

The proposed use pattern involves the use of a maximum of 0.5 lbs active ingredient per acre either as a preemergent or early postemergent application. For postemergence applications, FACET is to be applied with the addition of BCH 864 01 S, a spray adjuvant used to improve the consistency of weed control. (In a telephone conversation of 11/15/89, DEB was informed by BASF that the adjuvant consisted of a detergent and a solvent.) The PM should ascertain that these are cleared inerts.

FACET may be applied as an incorporated preplant, a preemergent, a delayed preemergent, or an early postemergent application. The timing of post emergent applications depends upon the size and growth stage of the specific weeds to be controlled. FACET may be applied to dry, moist, or saturated soils, but fields must be kept moist between application and permanent flooding. No more than 0.5 lbs. ai /A may be applied per season.

Under continuous flooding culture, FACET is to be applied to grasses and weeds under shallow flood conditions prior to raising of the water level. Under pin-point flooding culture, involving water-seeded rice, FACET should be applied about 5 days after water is drained but prior to flooding. The rice should have one visible leaf at application.

For preplant and postemergent applications in the rice growing areas of Arkansas, Louisiana, Mississippi, Missouri, and Texas the amount to be applied varies with the type of soil texture, ranging from a maximum of 0.34 lbs ai/A in coarse soils to 0.5 lbs ai/A in fine soils.

FACET may be applied by ground or aerially. For preplant and preemergence ground applications, volumes of 10 to 40 gallons of water per acre are recommended. For postemergent ground applications, in general 10 to 20 gallons/A are recommended with up to 30 gallons for dense crop and weed foliage.

Aerial applications calls for 5 gallons/A (10 gallons in California). The nozzle height is to be a maximum of 10 feet above the crop with nozzles oriented to discharge straight back into the airstream. Nozzle orientation should be at some angle between straight back and straight down. However, for optimum coverage, all nozzles should be oriented straight down. For preemergent and early postemergent use in Southern rice growing areas, FACET may be tank-mixed with thiobencarb or propanil. These herbicides are registered for use on rice.

Water from rice cultivation treated with FACET is not to be used to irrigate food or feed items unless FACET is registered for use with theses crops.

FACET is not to be applied to irrigation systems. Rice may be immediately replanted in treated fields. Small grains may be replanted after 3 months. All other crops may be replanted after 10 months.

The proposed label does not have a restriction upon using treated fields for aquaculture. Such a restriction is needed if the petitioner does not present residue data for catfish and crayfish. Alternatively the petitioner can determine residues in catfish and crayfish raised in treated fields and propose tolerances for these commodities if necessary.

Nature of the Residue

Plants Metabolism

The metabolism of quinclorac was studied by treating rice with ^{14}C ring-labeled material. The radiolabeled material was synthesized by reacting 3-chloro-2-methylaniline with U^{14}C glycerol followed by chlorination and oxidation. The procedure resulted in quinclorac labeled in the 2, 3, and 4 carbons of the quinoline ring. Radiochemical purity was 99% and chemical purity 98%. The specific activity was 9.74 mCi/mM (89,330 dpm/mcg).

In a growth chamber study, the labeled material was sprayed on rice at the 4-leaf stage at a rate of 1.34 lbs/A (about 3X the proposed rate). The above ground plant parts were harvested at maturity 97 days after application.

Straw (25 grams) was ground with dry ice and extracted with acetone/water. The filtrate was evaporated and redissolved in acetone/water. An aliquot was extracted with ether overnight. A portion of the ether extract was directly examined by TLC. Another portion of the ether extract was treated with methanolic HCL before examination by TLC.

Grain from the growth chamber studies was refluxed for 2 hours with water. After cooling, the solution was acidified and extracted with ether in a continuous extractor for 8 hours. The ether extract was concentrated, and extracted with 1 N NaOH. The aqueous phase was acidified and reextracted with ether. The ether extract was evaporated and the residue dissolved in methanol. Portions of the methanol extract were examined by TLC and GC-MS. For GC-MS, an aliquot of the methanol extract was reacted with methylanilinium hydroxide.

In a field study, rice was grown in a contained aluminum frame at Greenville Mississippi. The rice plant at the 3-5 leaf stage was treated with radiolabeled quinclorac at a rate of 0.75 lbs ai/A (1.5X the proposed label rate). A week after application a permanent flood was established. Above ground plant parts were harvested at intervals and at 118 days after application the remaining plants were harvested.

Whole field-grown plants sampled 28 days after treatment were ground with dry ice and extracted with acetone/water. The extract was concentrated and then acidified with HCl. This solution was extracted with dichloromethane followed by extraction with ethyl acetate. The combined organic extract was evaporated to dryness and the residue dissolved in acetone. A portion o the acetone extract was examined by TLC. The remaining acetone extract was evaporated and the residue treated wit diazomethane. The methylated material was also examined by TLC.

Rice grain from the final harvest of field grown plants was ground with dry ice and homogenized with hexane. The marc was dried and a portion redissolved in 1 N HCL by refluxing. The resulting solution was extracted with ether followed by ethyl acetate. The organic phases were

combined, evaporated to dryness, and redissolved in methanol. A portion was assayed by TLC while another portion was treated with diazomethane and also subjected to TLC.
Radioactivity was assayed in solid samples by LSC after combustion using a biological oxidizer. Liquid samples were directly analyzed for radioactivity by LSC.

Results

The straw from the growth chamber studies contained the radioactive equivalent of 12.79 ppm quinclorac. The final ether extract contained the radioactive equivalent of 11.18 ppm or 87.4% of the initial radioactivity of the straw. Ninety-nine percent of the radioactivity was identified as quinclorac. When the material was methylated, 99% was identified as the methyl ester of quinclorac.

The grain from the growth chamber studies contained the radioactive equivalent of 1.52 ppm quinclorac. The final ether extract contained 94% of the initial radioactivity of the grain. TLC demonstrated 100% of the applied radioactivity in a single peak with a Rf indicative of quinclorac. GC-MS of the methyl ester of the material in the final ether extract gave a mass spectrum identical to that of authentic methyl quinclorac.

In field treated rice the radioactive equivalent of 0.49 ppm quinclorac was found in the whole plant 28 days after treatment. 89.2% of this radioactivity was found in the final acetone extract with 8.2% in the marc. Of the extracted material 95% was identified as quinclorac. After methylation, 93% was identified as the methyl ester of quinclorac.

Harvest grain (PHI of 118 days) contained the radioactive equivalent of 0.12 ppm quinclorac. 83.5% was recovered in the final organic solvent extract and identified as quinclorac or its methyl ester.

Conclusion

When quinclorac is applied to plants the predominant component of the residue is the parent material itself. DEB concludes that the residue of regulatory concern in plants is quinclorac, per se.

Animal Metabolism

Lactating Ruminant

Radioactive quinclorac for administration to a goat was prepared by diluting ^{14}C ring-labeled quinclorac with cold material to yield quinclorac with a specific activity of 1.3 microcurie/mg. (2884 DPM/microgram). The ^{14}C-labelwas located in the 2, 3, and 4 positions of the quinoline ring. The positions of the of the labeled carbon atoms make it unlikely that major metabolites would be undetected.

An adult, lactating goat was given 1600 mg (equivalent to 800 ppm in the diet) of radiolabeled quinclorac in gelatine capsules daily for 5 days. An untreated animal served as control. The animals were housed in metabolism cages and were fed a conventional ration. Urine and feces were collected separately at 24 hour intervals. The goats were milked daily prior to dosing and 6 hrs. afterwards. Samples of blood were obtained just prior to dosing and at hourly intervals (6) after the last dose.

The goats were sacrificed 6 hours after the last dose and liver, kidney, muscle, fat, urine, and bile samples obtained. Radioactivity in aliquots of the samples was determined directly in liquid samples and after combustion for the solid tissues. Fecal samples and milk were extracted with methanol.

The residues after these extractions were combusted and examined for radioactivity. The methanol extracts were reduced in volume, acidified, and chromatographed on C_8 Band-Elut columns. Aliquots of the material eluted with ethyl acetate were directly counted and subjected to TLC. Urine sample were directly subjected to TLC. Standards of ^{14}C ring-labeled quinclorac were cochromatographed with samples.

Aliquots of kidney and liver tissues were homogenized with acidified ethyl acetate. Aliquots of the ethyl acetate layer were either counted directly or subjected to TLC. Tissue residues were combusted and counted.

Fat and muscle was chopped and extracted with alkaline 90% methanol and reextracted with methanol. The methanolic extracts were combined and aliquots of extracts and residues counted directly. The remaining methanolic extracts were subjected to Band-Elut chromatography, eluted with ethyl acetate and subjected to TLC.

Sixty-six percent of the total administered radioactivity was unabsorbed and excreted in urine and feces. Chromatography showed that 95% of the urinary radioactivity was unchanged quinclorac. Excretion in the milk accounted for 0.003% of the administered dose. The concentration in milk expressed as quinclorac ranged from 0.03 to 0.06 ppm. Methanol extracted 97% of the sample radioactivity. TLC chromatography showed that a single major peak corresponding to quinclorac which accounted for 87% of the radioactivity applied to the TLC plate.

The concentrations in tissues, expressed as quinclorac, were: kidney 10.3 ppm, liver 2.1 ppm, muscle 0.19 and 0.16 ppm, and fat 0.78 and 0.14. Eighty-two to 100% of the radioactivity in the tissues was extractable. Chromatography showed that greater than 90% of this radioactivity was in a single peak migrating the same as reference quinclorac. In some instances a minor peak, later identified as the glucuronide of quinclorac, and amounting to about 5% of the scanned radioactivity was seen.

Laying Hens

Radioactive quinclorac for administration to laying hens was prepared by diluting ^{14}C ring-labeled quinclorac with cold material to yield quinclorac with a specific activity of 1.24 microcurie/mg. (2774 DPM/microgram, 45.8 KBq/mg). The ^{14}C-label was located in the 2, 3, and 4 positions of the quinoline ring.

Laying hens (7) were given 80 mg (equivalent to 800 ppm in the diet) of radiolabeled quinclorac in gelatine capsules daily for 5 days. Five untreated hens served as controls. The animals were housed in stainless steel cages and were fed a conventional ration. Excreta and eggs were collected at 24 hour intervals.

The hens were sacrificed 6 hours after the last dose and liver, kidney, muscle, and fat samples obtained. Radioactivity in aliquots of the samples was determined directly for egg contents and after combustion for solid tissues. Excreta samples from 5 birds were extracted with methanol, an aliquot examined for radioactivity, and residues combusted and examined for radioactivity. Another aliquot was subjected to TLC chromatography.

Egg homogenates, muscle, and fat were extracted with methanol. The methanol extracts were reduced in volume, acidified, and chromatographed on C_8 Band-Elut columns. Aliquots of the material eluted with ethyl acetate were directly counted and subjected to TLC. Liver samples were extracted with ethyl acetate and aliquots were directly subjected to TLC. Standards of ^{14}C ring-labeled quinclorac were cochromatographed with samples.

About 93% of the total administered radioactivity was unabsorbed and excreted mainly as quinclorac. Chromatography showed that about 90% of the excreted radioactivity was unchanged quinclorac.

Concentrations in eggs ranged from <0.06 to 1.2 ppm. Methanol extracted 80 to 90% of the radioactivity in the eggs. TLC chromatography showed that a single major peak corresponding to quinclorac which accounted for 89 - 91% of the radioactivity of the egg extracts.

The concentrations in tissues, expressed as quinclorac, were: kidney 0.77 to 89 ppm, liver 0.26 to 10.53 ppm, muscle <0.05 to 4.22 ppm, and skin and fat 0.17 to 7.20 ppm. Eighty-nine to 98% of the radioactivity in the tissues was extractable. Chromatography showed that about 90%

of the total tissue radioactivity was in a single peak migrating the same as reference quinclorac. (In liver what appears to be a shoulder can be seen in the peak migrating with the cochromatographed standard. This may be an artifact or may represent another component. However for the purposes if this petition we will consider the parent as the metabolite of concern in poultry liver.) In some instances a minor peak, identified as the glucuronide of quinclorac, and amounting to about 5% of the scanned radioactivity was seen.

Conclusion

When quinclorac is fed to animals and poultry the predominant component of residues in tissues, milk, and eggs is quinclorac itself.

DEB concludes that the residue of concern for plants and for animals is quinclorac, per se.

Analytical Methods

Plant Matrices

Residues of quinclorac in rice grain, straw, hulls, bran, and polished grain were determined using BASF method A8902. The method is a revision of BASF's Method 226 and employs GC determination of the methylated derivative of the parent compound, per se.

Ten grams of finely ground sample material is allowed to swell in 100 ml of 0.1 N NaOH for 1 hour. The material is macerated with 200 ml of acetone using a high-speed blender and the resulting solution filtered through Celite with aspiration. The filtrate is acidified and concentrated to 75 ml using a waterbath and rotary evaporator. The concentrated aqueous solution is brought to pH 8.0 with sodium bicarbonate and adjusted to 500 ml. A 100 ml aliquot is extracted 3 times with 100 ml of dichloromethane. The remaining aqueous phase is acidified to pH 1-2 and extracted 3 times with dichloro-methane. The organic phases are combined, filtered and taken to dryness. The residue is redissolved in ether and methanol, treated with diazomethane, and taken to dryness. The methylated residue is dissolved in 75% dichloromethane /hexane and cleaned up on a silica gel column. The eluant fraction containing the methylated quinclorac is evaporated to dryness and redissolved in acetone/hexane. An aliquot is subjected to GC chromatography using DB-5 as the stationary phase and electron capture as the means of detection. Methylated standard and fortified samples are run in sequence with the unknowns. Quantitation of the analyte is by comparison of peak heights. Values are not corrected for blank controls or recoveries.

Recoveries from rice matrices spiked with 0.5 to 5.0 ppm quinclorac ranged from 76% in rice hulls and bran to 93% for brown rice with an average recovery of 81 ± 11%. The limit of determination is given as 0.05 ppm.

Animal Matrices

Residues of quinclorac in animal and poultry tissues were determined using BASF Method 268/1. The method is a revision of BASF's Method 268 and employs GC determination of the methylated derivative of the parent ingredient.

Twenty grams of sample material is homogenized with 150 ml of acetone and 100 ml of 0.1 N NaOH. The suspension is acidified, centrifuged, reextracted, and the supernatants filtered and made to volume. A 50 ml aliquot of the filtrate is concentrated to 15 ml using a waterbath and rotary evaporator.
The concentrated aqueous solution is added to an Extrelut column and eluted with ethyl acetate. The eluate is treated with a saturated sodium bicarbonate solution, the resulting aqueous phase is acidified with sulfuric acid and quinclorac extracted into dichloromethane.

The organic phase is added to an amino SPE column. Quinclorac is eluted from the column with pH 1.5 citrate buffer. Quinclorac in the eluate is partitioned into dichloromethane and the organic phase volume reduced to 2 -3 ml. This is treated with diazomethane, and taken to dryness. The methylated residue is dissolved in 75% dichloromethane /hexane and cleaned up on a silica gel column. The eluant fraction containing the methylated quinclorac is evaporated to dryness and redissolved in acetone/hexane. An aliquot is subjected to GC chromatography using DB-5 as the stationary phase and electron capture as the means of detection. Methylated standard and fortified samples are run in sequence with the unknowns. Quantitation of the analyte is by comparison of peak heights. Values are not corrected for blank controls or recoveries.

Recoveries ranged from 64% for liver spiked with 5 ppm to 90% for cow's milk spiked at 0.05 ppm. The limit of determination is given as 0.05 ppm.

Validation of Methods

The Agency's Analytical Chemistry Section has conducted method validations of the plant and of the animal analytical procedures with the following results:

Matrix	Fortification Levels	Recoveries
Rice Grain	5 and 10 ppm	96 - 113%
Rice Straw	12 and 24 ppm	86 - 96%
Rice Bran	15 and 30 ppm	88 - 96%
Chicken Liver	0.1 and 0.2 ppm	69 - 107%
Beef Liver	0.05 and 0.1 ppm	83 - 119%
Milk	0.05 and 0.1 ppm	71 - 110%
Eggs	0.05 and 0.1 ppm	62 - 86%

The limits of detection are estimated as 0.05 ppm for plant tissues and 0.025 to 0.05 ppm for animal tissues.

(See C. Corley and K. T. Zee, memo, 4/23/90; D. Swineford, E. Greer, C. Stafford, and M. Law, memo 4/23/90; and E. Greer, C. Stafford, and D. Swineford, memo 4/6/90.)

We conclude that the proposed analytical methods are suitable for enforcement purposes.

Storage Stability

Storage stability was determined by fortifying untreated field samples of plant matrices. Rice and soybean grain, rice straw, and corn forage were chopped and finely ground . After being fortified to 1 ppm with quinclorac, the samples were placed in a freezer for 8 months along with unfortified samples. At this time the samples were analyzed for quinclorac along with frozen control samples fortified at 1 ppm on the day of analysis. The results were as follows:

Matrix	"0" day	8 Months	Stability
Rice Grain	0.76	0.82	108%
Rice Straw	0.77	0.92	119%
Corn Forage	0.93	0.85	91%
Soybean Grain	0.75	0.80	107%

We conclude that the stability of quinclorac over 8 months in plant matrices has been demonstrated.

Storage stability in animal tissues was assessed by reanalyzing tissue samples for quinclorac after a period of time equal to their storage prior to the initial analysis. It was shown that quinclorac residues ware stable over this period. Stability in animal and plant tissues was also demonstrated in the accountability studies where plant and animal tissues were stored for 3 years between radiochemical and chromatographic analyses.

Accountability of Analytical Methods

Samples of plant and animal tissues containing radioactive metabolites of quinclorac were subjected to the proposed analytical methods for quinclorac. The radioactive material had been demonstrated to be predominantly parent in the metabolism experiments described above. In the accountability studies the amounts determined as quinclorac by the chemical methodologies were compared to the total recoverable radioactivity (TRR) in the samples as determined by combustion and LSC.. Analytical procedure A8902 was used for the plant tissues; analytical method 268 for chicken tissues and eggs; and analytical method 268/1 for goat tissues and milk. The values for accountability were corrected for recoveries. The results were as follows:

Matrix	% of TRR recovered in analytical method
Rice	
Grain	95
Straw	106
Forage	85

Matrix	% of TRR recovered in analytical method
Goat	
Liver	62
Muscle	79
Milk	83
Chicken	
Muscle	84
Skin and Fat	88
Kidney	88
Liver	73
Eggs	66

We conclude that the accountability of the analytical methods has been demonstrated.

Behavior of Quinclorac in Multi-residue Methods

Quinclorac was not detected by the procedures of protocols I, II, II, or IV of the FDA multi-residue methods. In protocol IV an intrinsic fluorescence of quinclorac was found.

Magnitude of the Residue

Plants

Nine rice growing trials were conducted in Arkansas, California, Louisiana, Mississippi, and Texas, encompassing the major rice growing areas of the US. Applications of 0.5 to 0.7 lbs active were made by ground or by aerial application. Applications were made to non-flooded field except in California where 1 to 2 inches of water were in the fields and plants were at a later growth stage. Rice was harvested at normal maturity, 76 to 98 days after application. Samples were frozen and shipped to BASF for analysis. Analyses were done after 4 or 5 months of frozen storage. Storage for this period has demonstrated stability in quinclorac residues. Analyses were made by method A8902 for plant matrices. The limit of quantitation is 0.05 ppm. Recoveries averaged 88±14% for rice grain and 94±15 for rice straw. Residue levels of quinclorac were not corrected for recoveries. Results were as follows:

Site	Rate	PHI	Method	Residue Range
Rice Grain				
California 1	0.5	77	Aerial	1.5
	0.5-0.7	77	Ground	1.9-4.3
California 2	0.5	77	Aerial	1.6
	0.6	77	Ground	2.2
Texas 1	0.5	77	Aerial	<0.05
	0.5	77	Ground	0.06-0.07
Texas 2	0.5	76	Aerial	0.12
	0.5	76	Ground	0.08-0.09
Texas 2	0.5	174	Aerial	<0.05
(Ratoon)	0.5	174		<0.05
Arkansas 1	0.5	76	Aerial	<0.05
	0.5	76	Ground	0.09-0.10
Arkansas 2	0.5	80	Aerial	0.12
	0.5	80	Ground	0.22
Louisiana 1	0.5	98	Aerial	<0.05
	0.5	98	Ground	<0.05-0.08
Louisiana 2	0.5	76	Aerial	0.08
	0.5	76	Ground	<0.05-0.15
Mississippi	0.5	78	Aerial	<0.05
	0.5	78	Ground	0.06-0.16

Site	Rate (lb ai/A)	PHI (days)	Method	Residue Range (as ppm quinclorac)
Rice Straw				
California 1	0.5	77	Aerial	2.6
	0.5-0.7	77	Ground	3.2-11.1
California 2	0.5	77	Aerial	4.0
	0.6	77	Ground	4.0-6.7
Texas 1	0.5	77	Aerial	0.12
	0.5	77	Ground	0.10-0.47
Texas 2	0.5	76	Aerial	0.18
	0.5	76	Ground	0.18-0.23
Texas 2 (Ratoon)	0.5	174	Aerial	<0.05
	0.5	174		<0.05
Arkansas 1	0.5	76	Aerial	0.14
	0.5	76	Ground	0.39-0.46
Arkansas 2	0.5	80	Aerial	0.23
	0.5	80	Ground	0.23-0.24
Louisiana 1	0.5	98	Aerial	0.08
	0.5	98	Ground	0.05-0.11
Louisiana 2	0.5	76	Aerial	0.30
	0.5	76	Ground	0.09-0.53
Site	Rate (lb ai/A)	PHI (days)	Method	Residue Range (as ppm quinclorac)
Mississippi	0.5	78	Aerial	<0.05
	0.5	78	Ground	<0.05-0.11

In general ground application resulted in higher residues than aerial application. The greatest residue levels were 4.3 ppm for grain and 11.1 ppm for straw in the California trials at slightly exaggerated rates (0.7 lb ai/A). Based on these results,the petitioner has proposed 5 ppm as the quinclorac tolerance for rice grain and 12 ppm as the tolerance for rice straw.

Rice Processing Study

Quinclorac was applied to a rice field in Texas at an exaggerated rate of 1.5 lb ai/A (3X) and the rice harvested at a PHI of 79 days. The rough rice was sent to the Rice Research Center of the USDA at Beaumont Texas and processed. Samples of the original rice and processed fractions were transferred to the BASF laboratories and placed in frozen

storage. After 13 months of storage, the samples were analyzed by Method A8902 for quinclorac residues with the following results:

Fraction	Quinclorac Residues ppm
Rough Rice	0.46
Rice Hulls	0.47
Brown Rice	0.46
Rice Bran	1.4
Milled Rice	0.34

As residues concentrated only in the bran fraction and by a factor of 3, the petitioner is proposing a food/feed additive tolerance of 15 ppm for rice bran.

We note that 8 months was the length of the storage time in the storage stability studies previously described. In the rice processing studies, the fractions were stored for 13 months. The petitioner indicates that they are aware of this and that they are conducting studies of storage stability for the longer interval.

Animal Tissue Residues

Rice grain and rice straw can be feed items for cattle and poultry. As a consequence the petitioner has conducted cattle and poultry feeding studies and has proposed tolerances for cattle and poultry tissues and for milk and eggs.

Lactating Cattle

Lactating cows were feed a standard ration and dosed daily with quinclorac at the equivalent of 1, 10, 100, or 500 ppm in their diet. Milk was obtained daily. This regimen was maintained for 28 days at which time the cows were sacrificed and tissues examined for quinclorac residues by method 268/1. The results were as follows:

Tissue	Quinclorac Residues Feeding Level (ppm)			
	1	10	50	500
Liver	<0.05	<0.05	<0.05	0.19-0.33
Kidney	<0.05	0.08	0.19	1.2-2.6
Fat (subcut.)	<0.05	<0.05	<0.05	0.12-1.14

Tissue	Quinclorac Residues Feeding Level (ppm)			
	1	10	50	500
Fat (periton.)	<0.05	<0.05	<0.05	0.20-0.27
Muscle	<0.05	<0.05	<0.05	<0.05
Milk	<0.05	<0.05	<0.05	<0.05

0.05 ppm is considered the limit of quantitation for the method. Recoveries averaged 80±11%. The results are not corrected for recoveries.

Cattle can consume 20 kg dry matter per day. Rice grain can constitute 25% of the feed for dairy cattle and rice straw can be 10% of the feed of beef cattle. Assuming the proposed tolerance levels, this would amount to 25 mg daily for dairy cattle (0.25 x 20 kg x 5 mg/kg) and 24 mg for beef cattle (0.1 x 20 kg x 12 mg/kg). The 2 lowest feeding levels in the feeding study were 1 ppm and 10 ppm. At 20 kg consumed per day this is equivalent to 20 and 200 mg quinclorac per day.

As the higher value is 8 fold greater than that expected from the proposed tolerance levels, we will assume that tissue levels at 200 mg per day will indicative of levels to be expected at the proposed rice grain and rice straw tolerances. At this feeding level all tissue and milk residues were below the limit of quantitation of 0.05 ppm. As a consequence the petitioner has proposed tolerances of 0.05 ppm for cattle, goat, horse, and sheep fat, meat, and meat by-products.

DEB considers that the tolerances are appropriate.

Laying Hens

Laying hens were feed a standard ration and dosed daily with quinclorac at the equivalent of 1, 10, or 100 in their diet. Eggs were obtained daily. This regimen was maintained for 28 days at which time the hens were sacrificed and tissues examined for quinclorac residues by method 268/1. The results were as follows:

Tissue	Quinclorac Residues Feeding Level (ppm) 1	10	100
Eggs	<0.05	<0.05	<0.05
White Muscle	<0.05	<0.05	<0.05-0.07
Brown Muscle	<0.05	<0.05	<0.05
Liver	<0.05	<0.05	<0.05-0.13
Kidney	<0.05	<0.05	0.21-0.56
Skin and Fat	<0.05	<0.05	0.12-0.76
Heart	<0.05	<0.05	<0.05-0.06
Gizzard	<0.05	<0.05-0.17	<0.05-1.2

0.05 ppm is considered the limit of quantitation for the method. Recoveries averaged 81±13%. The results are not corrected for recoveries.

Laying hens can consume 150 grams of dry feed per day. Rice grain can constitute 40% of the feed for poultry. Assuming the proposed tolerance levels, this would amount to 0.3 mg daily for poultry (0.4 x 0.15 kg x 5 mg/kg). The 2 lowest feeding levels in the feeding study were 1 ppm and 10 ppm. At 0.15 kg feed consumed per day this is equivalent to 0.15 and 1.5 mg quinclorac per day. As the higher value is 5 fold greater than that expected from the proposed tolerance levels, we will assume that tissue levels at 1.5 mg per day will be indicative of levels to be expected at the proposed rice grain tolerance. At this feeding level eggs and all tissue except the gizzard were below the limit of quantitation of 0.05 ppm. As a consequence the petitioner has proposed tolerances of 0.05 ppm for eggs and poultry fat and meat and 0.10 ppm for poultry meat by-products.

DEB considers that the proposed tolerances are appropriate.

Other Tolerances

There are no Codex, Canadian, or Mexican tolerances for quinclorac.

cc with CBI: PM-25, R.F., PP#3755, S.F., Reviewer, FOD/PIB (Furlow)
cc without CBI: Circ.
RDI:PE:8/1/90:RAL:8/2/90
H7509:DEB:JG:jg:8/2/90:CM#2:803c:557-1405

RIN 2679-96

Quinclorac

Page_____ is not included in this copy.

Pages 25 through 29 are not included.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

✓ Description of the product manufacturing process.

✓ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

_____ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

Attachment: Page___ of___

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL QUINCLORAC

CODEX NO. _____

CODEX STATUS:

[X] No Codex Proposal Step 6 or Above

Residue (if Step 8): _____

Crop(s)	Limit (mg/kg)

CANADIAN LIMITS:

[X] No Canadian Limit

Residue: _____

Crop(s)	Limit (mg/kg)

PROPOSED U.S. TOLERANCES:

Petition No. 9F3755/9H5583

DEB Reviewer JG

Residue: 3,7-DICHLORO-8-QUINOLINE CARBOXYLIC ACID

Crop(s)	Limit (mg/kg)
RICE GRAIN	5
RICE STRAW	12
CATTLE FAT, MEAT, BYP	0.05
GOAT " " "	0.05
HOGS " " "	0.05
HORSE " " "	0.05
SHEEP " " "	0.05
POULTRY FAT & MEAT	0.05
POULTRY MBYP	0.10
MILK & EGGS	0.05

MEXICAN LIMITS: RICE BRAN 15 C

[X] No Mexican Limit

Residue: _____

Crop(s)	Limit (mg/kg)

NOTES

Form Revised 1989