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

FEB 4 1986

OFFICE OF  
PESTICIDE AND TOXIC SUBSTANCES

MEMORANDUM

**EXPEDITE**

SUBJECT: PP#6F3316. (RCB Nos. 111, 112, and 113).  
Fenoxaprop-ethyl (HOE 33171) on Soybeans and  
Rice. Evaluation of Analytical Methods and  
Residue Data (Accession Nos. 258947, 073950,  
073951, 073955, 073956, 073957, 073958,  
073959, 073960).

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Tolerance Petition Section II  
Residue Chemistry Branch  
Hazard Evaluation Division (TS-769C)

THRU: Charles L. Trichilo, Chief  
Residue Chemistry Branch  
Hazard Evaluation Division (TS-769C)

TO: Richard Mountfort, Product Manager #23  
Fungicide-Herbicide Branch  
Registration Division (TS-767C)

and

Toxicology Branch  
Hazard Evaluation Division (TS-769C)

Note: This review was expedited as stated in the letter of  
November 1, 1985 from D. Campt, Director, Registration Division.

American Hoechst Corporation proposes the establishment of  
tolerances for residues of the herbicide fenoxaprop-ethyl [(+)-  
ethyl 2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]propanoate] and  
its metabolites 2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy] propanoic  
acid and 6-chloro-2,3-dihydrobenzoxazol-2-one, calculated as  
parent, in or on soybeans, rice, and rice straw at 0.05 ppm.

Temporary tolerances are established for rice grain and rice  
straw at 0.02 ppm and for soybean seed at 0.05 ppm. These  
temporary tolerances expire on April 4, 1986. No permanent  
tolerances are established for fenoxaprop-ethyl.

CONCLUSIONS

1. One inert is not cleared for the proposed use on rice. The petitioner must formally ask for an exemption from the requirement of a tolerance for one of the inerts when used on rice. Refer to the Confidential Appendix of this review.
2. The proposed tank mixing of fenoxaprop-ethyl with Blazer<sup>®</sup> 2L and Basagran<sup>®</sup> 4 SL are prohibited by restrictions which Rohm and Haas Company and BASF Wyandotte Corporation have placed on their labels. The inclusion of Whip IEC on the Rohm and Haas and Wyandotte labels and/or the permission for American Hoechst Corporation to tank mix Whip IEC with Blazer<sup>®</sup> 2L and Basagran<sup>®</sup> 4SL needs to be resolved by these companies (the petitioner, Rohm and Haas, and BASF Wyandotte)(see the Proposed Use section of this review for further details).
3. Since Whip IEC contains [REDACTED] the inclusion of Whip IEC on the Rohm and Haas Propanil label and/or the permission for American Hoechst Corporation to tank mix Whip IEC with Propanil needs to be resolved by the petitioner and Rohm and Haas (see the Proposed Use section of this review for further details).
- 4a. In a soybean metabolism study, the petitioner has claimed that total radioactive fenoxaprop-ethyl residue in seeds was less than 0.005 ppm (PHI's 51 to 126 days); however, although the proposed analytical method has the capability to analyze about one-third of the terminal residue (after loss), the field studies (discussed later in this review) indicated that more total terminal residue could be present in seeds.
- 4b. Considering the structure, systemic properties, etc. for fenoxaprop-ethyl, RCB defers to TOX as to whether the identification of 55% and 28% of the residue in soybeans and rice, resp., is adequate for TOX considerations. Although the petitioner has made an effort towards understanding the metabolism of fenoxaprop-ethyl in soybeans, rice, and the lactating cow, RCB reserves any final conclusion until TOX has had a chance to comment on this issue. If TOX feels that further identification of residues is needed for toxicological considerations, then the petitioner should do further metabolic work. In order to further identify the nature of the <sup>14</sup>C activity, the petitioner may want to consider, among various possibilities, the following: exhaustive reflux extraction with HBr or HI instead of HCl; exhaustive extractions with other solvents such as ether, acetone, etc.; enzymatic hydrolysis; column chromatography of polar residues in the water phase by gel permeation chromatography and/or ion-exchange chromatography; and electrophoresis of polar residues in the water phase. The preceding are only some suggestions. The petitioner, of course, will want to use the best available technology in order to provide the necessary metabolism understanding.

INFORMATION WHICH MAY REVEAL THE IDENTITY OF AN INERT INGREDIENT IS NOT INCLUDED

- 5a. The petitioner uses hydrochloric acid as a cleaving agent for plant residues with the intent of converting the parent compound and the metabolite HOE 53022 to HOE 54014 (6-chloro-2,3-dihydrobenzoxazol-2-one) which is also one of the metabolites that was defined. But, is HCl the right choice of acid for cleaving the preceding compounds? One notices that etheral bonds (-O-) are located at two positions in HOE 33171 and HOE 53022. According to March (Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, p. 344, McGraw-Hill, New York, 1968) the following is stated:

"Ethers may be cleaved by heating with concentrated HI or HBr. HCl is seldom successful. HBr reacts more slowly than HI, but it is often a superior reagent since it causes fewer side reactions."

- 5b. At this time, RCB will reserve its conclusion on the acceptance of the proposed analytical methodology for regulatory purposes until RCB has received an answer to its deference to TOX concerning the adequacy of the characterization of residues for toxicological consideration and/or the nature of the residue in plants and animals is finalized. More work may need to be done on the proposed analytical methodology.
- 5c. RCB has requested (January 8, 1986 telephone conversation between N. Dodd - EPA and William Horton - American Hoechst Corp.) the petitioner to submit the metabolic standards HOE 53022 and HOE 54014 to its North Carolina depository in preparation for an EPA method trial. Although the analytical procedure is questionable, RCB will submit it for a method trial. After TOX has answered RCB's deference concerning the toxicological significance of the residue and work has been finalized on the proposed regulatory procedure, a final determination will be made as to what residues need to be regulated.
- 6a. RCB concludes that adequate storage stability data are available for the parent compound fenoxaprop-ethyl only.
- 6b. Since it appears that fenoxaprop-ethyl is highly systemic and much more of the metabolites are present in the terminal residues of weathered crops than the parent compound, the petitioner should also submit storage stability data for those major metabolites that will be regulated. At this time, we do not know what these regulated metabolites will be since more metabolic work may need to be done.

- 7a. At this time, RCB must reserve its conclusion on the adequacy of the proposed 0.05 ppm fenoxaprop-ethyl tolerance on soybeans and possibly soybean fractions; more work may have to be done on plant metabolism and the analytical procedure that is proposed for regulatory purposes. The petitioner should be informed that it may be necessary for him to reanalyze some of his reserve field soybean samples as a result of the preceding work. Also, if the storage stability data for the parent and major metabolites are not adequate, then new field residue data may need to be generated.
- 7b. The recovery/validation data for fenoxaprop-ethyl in soybeans/soybean fractions could be misleading even though at face value most of them would seem to be acceptable. Generally, RCB will approve of validation data where the concerned residues necessary for regulation are added to the samples before analyses, but there must be a good correlation between the accountable residues in the metabolism study and the accountable residues recovered by the proposed analytical procedure.
8. In view of the above, RCB reserves its final conclusion concerning the adequacy of the proposed 0.05 ppm fenoxaprop-ethyl tolerance on rice grain and straw; more work may have to be done on the plant metabolism and the proposed analytical procedure for regulatory purposes. The petitioner should be informed that it may be necessary to reanalyze some of his reserve field rice samples as a result of the preceding work; the storage stability study on both the parent compound and the major metabolites must be adequate in order to accept these data from reanalyses. Otherwise, it may be necessary to generate some new field residue data.
- 9a. No cattle or poultry feeding studies have been submitted. Soybeans, soybean hulls, rice straw, and hulls may be fed to livestock.
- 9b. RCB must reserve its conclusion on the immediate need for cattle and poultry feeding studies until the plant metabolism, proposed analytical methodology, and field residue studies have been considered adequate.
10. An International Residue Limits (IRL) Status sheet is attached. There are no Codex, Canadian, and Mexican tolerances for fenoxaprop-ethyl on soybeans and rice. Therefore, no compatibility questions exist with respect to Codex.
11. The identity of HOE S1728 (ATA TH-T of the Hoechst Company), which is an emulsifier solution used in the analytical method, is needed.
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RECOMMENDATIONS

RCB recommends against the establishment of the proposed tolerance of 0.05 ppm fenoxaprop-ethyl on soybeans, rice, and rice straw for reasons given in Conclusions 1, 2, 3, 4a, 4b, 5a, 5b, 5c, 6b, 7a, 7b, 8, 9b, and 11 above.

RCB recommends that an unabridged copy of this review be sent to the petitioner; he should read all RCB's Comments and Conclusions set forth in this review.

DETAILED CONSIDERATIONSManufacture

The manufacture of technical fenoxaprop-ethyl (HOE 33171) was discussed in RCB's review of PP#3G2940 (R. Loranger, November 9, 1983). The technical contains at least 93.0% active ingredient. RCB does not expect the impurities in the technical to cause a residue problem. Refer to the Confidential Appendix for a summary of the manufacturing process and impurities.

Formulation

The formulation to be used on rice and soybeans is Whip<sup>®</sup> IEC Herbicide, an emulsifiable concentrate containing 1 lb ai/gal, or 12.50% fenoxaprop-ethyl/gal and 87.50% inerts. One inert is not cleared for the proposed use on rice but is cleared for the proposed use on soybeans. The petitioner must formally ask for an exemption from the requirement of a tolerance for that inert when used on rice. The other inerts are cleared under 40 CFR 180.1001 (c) or (d). Refer to the Confidential Appendix for a discussion of the inerts in the formulation.

Proposed UseSoybeans

Apply 0.1 to 0.2 gal Whip IEC/A (0.1 to 0.2 lb ai/A) to grassy weeds to thoroughly cover the weeds when the weeds are 3 to 16 inches tall, depending on the grass species. Apply by ground in a minimum of 10 gal water/A or by air in a minimum of 5 gal water/A. One quart Crop Oil Concentrate per acre with ground applications or 1 pint Crop Oil Concentrate per acre with aerial applications is either required, optional, or prohibited, depending on grass species.

A second application may be necessary if new grass appears. Whip IEC can be applied as a spot treatment in a 1% vol/vol solution with water (i.e. 32 fl. oz. Whip IEC per 25 gal water). Apply Whip IEC Herbicide before the bloom stage of soybeans. Do not graze or feed treated forage, hay, or straw of soybeans.

Whip IEC Herbicide is also proposed to be tank mixed with Basagran<sup>®</sup> 4 SL or Blazer<sup>®</sup> 2L. Apply the tank mix by ground equipment in a minimum of 20 gals. spray solution/A or by aerial equipment in a minimum of 5 gal spray solution/A.

For tank mixes with Basagran<sup>®</sup> 4 SL (EPA Registration No. 7969-45), apply 1.2 to 1.6 pts. Whip IEC/A (0.15 to 0.2 lb ai/A) and 1.5 to 2.0 pts. Basagran 4 SL/A (0.75 to 1.0 lb. a.i./A) when annual grassy weeds are 1 to 8" tall. Do not tank mix Whip IEC Herbicide and Basagran if the annual grassy weeds have more than 2 tillers or

are larger than 8 inches tall. Special Note: For the control of shattercane 8 to 12" tall and broadleaf weeds that are on the Basagran label, tank mix Whip 1EC Herbicide at a rate of 1.2 pts./A (0.15 lb ai/A) with Basagran at 1.5 to 2.0 pts./A (0.75 to 1.0 lb ai/A). Do not use the tank mix of Whip and Basagran to control rhizome Johnsongrass. If the growth stages of the grassy and broadleaf weeds are not those specified on the Whip and Basagran labels, apply Whip and Basagran separately, observing a 3-day interval between the applications. Always add Crop Oil Concentrate at the rate of one quart/A for ground application and 1 pt/A for aerial application when tank mixing Whip 1EC Herbicide and Basagran for use on soybeans (only).

For tank mixes with Blazer<sup>®</sup> 2L Herbicide (EPA Registration No. 707-150 AA), apply 1.6 pts. Whip 1 EC/A (0.2 lb. a.i./A and 1.5-2.0 pts. Blazer 2L/A (0.375 to 0.5 lb ai/A). Do not use any formulation of Blazer other than the 2L formulation. Do not use Crop Oil Concentrate or any other surfactant with the tank mix of Whip and Blazer 2L. Do not use the tank mixture of Whip and Blazer 2L for control of rhizome Johnsongrass. If the growth stages of the grassy and broadleaf weeds are not those on the labels, apply Whip and Blazer separately, observing at least a 3-day interval between Whip and Blazer applications if Whip is applied first or at least a 7-day interval between Blazer and Whip if Blazer is applied first.

### Rice

Apply Whip 1EC by ground or air in a minimum of 10 gal water/A. Apply in the states of AR, LA, MS, MO, TX, and CA at the rate of 1.2 to 1.6 pts. Whip 1 EC/A (0.15 to 0.2 lb ai/A), depending on weed size or weed growth stage. Rice is tolerant to Whip from the 4-leaf to the panicle initiation stage. Do not apply Whip after the panicle initiation stage of rice development. Do not make more than two applications of Whip 1EC per growing season. Do not use Whip on the rice varieties Mars and Leah, as damage to these species may occur. Rice straw and hulls may be fed to livestock.

Concerning tank mixes, Whip 1EC is proposed to be tank mixed with Basagran. (Refer to the tank mix recommendations for Basagran under "Soybeans" above.) Propanil is not proposed to be applied as a tank mix or sequentially within 6 days of the Whip application.

### Water Management for Rice in AR, LA, MS, MO, and TX:

For rice which is less than 8 inches high, do not flood rice fields for at least 7 days after the Whip 1 EC application. For rice which is more than 8 inches in height, the field can be reflooded in 4 to 5 days after the application. The water depth should not exceed 3 inches for at least 21 days after the Whip 1EC application. The permanent flood can be applied any time after

21 days following treatment.

For control of tillered grass, water levels at the time of application of Whip should not cover more than 25 percent of the rice and annual grass foliage.

Water Management for Rice in CA (only):

For early application, apply Whip 1 EC immediately after drainage of the rice basin. Reflooding of the basin should begin no sooner than 3 days after the Whip application.

For late application, apply after the rice is completely tillered. Maintain a water depth so that at least 80 percent of the rice and watergrass foliage is exposed at application. Reflood to a normal depth within 2 to 3 days after application.

RCB's Comments and Conclusions on the Proposed Label

Tolerances are established for bentazon (Basagran®) on soybeans, soybean forage, and soybean hay (40 CFR 180.355) and for acifluorfen (Blazer®) on soybeans at 0.1 ppm (40 CFR 180.383).

The published labels for Basagran® 4 SL and Blazer® 2L contain restrictions prohibiting tank mixing with any pesticides that are on the Basagran® or Blazer® labels. The label for Blazer® on soybeans contains the following use restrictions concerning tank mixes:

"Do not mix Blazer 2L herbicide with oils, liquid fertilizers, or pesticides except as specifically directed on this label or on other approved Rohm and Haas Company supplemental labeling."

The Wyandotte Corporation's label for Basagran® contains the following restriction concerning tank mixes:

"Do not mix or apply Basagran with any other pesticide or with fertilizer except as specifically recommended on this labeling."

The label for Propanil on rice (STAM LV-10, Rohm and Haas, EPA Registration No. 707-94-AA) contains the following restriction:

"Mix only with water and apply as a spray. Do not add oils, adjuvants, liquid fertilizer, or certain insecticides (see compatibility below), to do so may cause injury to rice."

RCB concludes the following concerning the rice and soybean labels:

1. The proposed tank mixing of fenoxaprop-ethyl with Blazer®

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2L and Basagran® 4SL are prohibited by restrictions which Rohm and Haas Company and BASF Wyandotte Corporation have placed on their labels. The inclusion of Whip IEC on the Rohm and Haas and Wyandotte labels and/or the permission for American Hoechst Corporation to tank mix Whip IEC with Blazer® 2L and Basagran® 4SL needs to be resolved by these companies (the petitioner, Rohm and Haas and BASF Wyandotte).

2. Since Whip IEC contains [REDACTED] the inclusion of Whip IEC on the Rohm and Haas Propanil label and/or the permission for American Hoechst Corporation to tank mix Whip IEC with Propanil needs to be resolved by the petitioner and Rohm and Haas.

### Nature of the Residue

#### Plants

Refer to the Glossary (Attachment 1) at the end of this review for structures, chemical names, and Hoechst code numbers for fenoxaprop-ethyl and its metabolites.

#### Soybeans

Two metabolism studies on soybeans (Hoechst Reports No. A25722 and A24553) have previously been reviewed in PP#3G2940, Accession No. 071799 (R. Loranger, November 9, 1983). (These studies are re-submitted in PP#6F3316, Accession No. 073956, as Tabs D-2, D-3, and D-4).

In the first study, <sup>14</sup>C-chlorophenyl-ring-labeled HOE 33171 was sprayed on soybeans at the two foliate leaf stage (28 days after planting) at the rate of 0.3 kg ai/hectare (0.27 lb. a.i./A). Plants were collected 0, 6, 14, 30, 51, 90, and 126 days after treatment. Total radioactivity in various plant parts was determined by combustion and measurement of <sup>14</sup>CO<sub>2</sub>. The treated leaves contained 25 to 80 ppm of activity equivalents of fenoxaprop-ethyl from days 0 to 51. New leaves had 3.9 ppm equivalents on day 6, 1.2 ppm on day 30, 0.13 ppm on day 51, 0.007 ppm on day 90, and 0.048 ppm at harvest (126 days). Treated stems had ca 3 ppm on day 0 and ca 0.1 ppm on day 90. The petitioner reports further that radioactivity in stems concentrated to 2 ppm at harvest due to dessication. On days 51, 90, and 126, dried pods contained 0.007 ppm and seeds contained no detectable radioactivity (< 0.005 ppm).

In the second study, soybeans at the 2 to 3 foliate stage were treated with <sup>14</sup>C-chlorophenyl-ring-labeled HOE 33171 at the rate of 0.3 kg ai/ha. Residues in the sprayed leaves after the plants were kept for 15 days in the greenhouse were characterized as follows:

<u>Compound</u>	<u>% of total <sup>14</sup>C</u>
HOE 33171	28.7
HOE 53022	4.7
HOE 67978	4.2 (2.4)*
HOE 64124	7.3 (7.3)*
HOE 54014	9.9 (9.9)*
10-12 unidentifieds**	21
mass > 1000	7
bound	18

\* ( ) - % conjugated

\*\* 0.2 to 6% each

A soybean metabolism study using a <sup>14</sup>C-label in the dioxyphenyl ring of HOE 33171 is submitted in this petition (Hoechst Report No. A30297, Tab D-5 of Accession #073956). Soybeans at the 2 to 3 foliate leaf stage were sprayed at the rate of 0.3 kg ai/ha. Residues in the treated leaves were characterized 14 days after treatment by thin layer chromatography and high performance liquid chromatography. Sixty-one point three percent of the total radioactivity was extractable and 33 percent was bound or unextractable. Residues, as a percentage of total radioactivity, were identified as follows:

29.2%	HOE 33171
12.2%	HOE 53022
2.3%	HOE 20686
1.1%	HOE 40356
13.4%	separated but unidentified compounds (at least 10)

A total of 8.8 percent of the radioactivity was lost during the analytical procedure. Leaves grown after treatment contained < 5 percent of the concentration in treated leaves.

### Rice

Two metabolism studies on rice (Hoechst Reports No. A27819 and A27834) have previously been reviewed in PP#4G3035 (R. Loranger, June 7, 1984). (These studies are resubmitted in PP#6F3316, Accession No. 073956, as Tabs D-6 and D-7).

In the first study, greenhouse-grown rice at the 4 to 5 leaf stage was treated with <sup>14</sup>C-chlorophenyl-labeled HOE 33171 one day after draining off the water. Treatment rates were 0.075 or 0.15 lb ai/A. Mature rice ears were collected 143 days after application. Green leaves were harvested on day 149 and straw on days 176 and 183. Residues in crop parts and processing fractions as determined by combustion to <sup>14</sup>CO<sub>2</sub> are given below:

Crop Part	PPM <sup>14</sup> C	
	0.075 lb ai/A	0.15 lb ai/A
Rough rice*	0.006	0.020
Brown rice	0.006	0.020
White rice	0.005	0.022
Hulls	0.005	0.018
Green leaves	0.014	0.026
Straw	0.01**	0.08**
		1.1***

\* Calculated from 80% brown rice plus 20% hulls

\*\* Portion 10 cm and higher above soil surface

\*\*\* Portion 0 to 10 cm above soil surface

In the second study, some residues were characterized. HOE 33171 was applied to greenhouse-grown rice at a growth stage between tillering and bolting. Two extraction schemes were tried, and the following was given:

"Extraction scheme A used homogenization with 1:1 methylene chloride-water. The filtrate separated into 2 phases with 5% of the radiolabel in the organic phase and 27% in the aqueous layer. Thus, 68% of the residue remained in the filter cake. Most of the organic activity (5% total residue) was identified by comparing  $R_f$  values with standards on silica gel TLC plates. In detail, the methylene chloride phase was evaporated, the residue dissolved in 7:3 methanol-water, and the resulting solution passed through a C-18 SEP-PAK prior to the thin layer chromatography. The parent compound ( $R_f = 0.67$ ) comprised 20% of the organic layer's activity (or 1.0% of the total radiolabel). HOE 54014 (component measured by analytical method) represented 1.2% of total activity with 1.8% associated with the carboxylic acid 53022, although the latter is close in  $R_f$  value to the hydroxylated benzoxazolones 64124 and 67978. The remaining 1.0% of the  $CH_2Cl_2$  activity was classified as unidentified highly polar compounds based on it being found at the TLC origin. The latter was also the case for all the activity (27% of total) in the aqueous phase of the filtrate.

The filter cake (68% <sup>14</sup>C) was refluxed with 4:1 HCl-ethanol and 82% of that residue (56% total <sup>14</sup>C) was solubilized. However, the TLC work resulted in all the material being at the origin as in the aqueous layers above. Thus, the total amount of activity identified via extraction scheme A is 4.0% (1.0% parent, 1.2% HOE 54014, 1.8% HOE 53022).

A second sample of rice leaves was refluxed directly with 4:1 HCl (1.2M)/ethanol (analytical method conditions) (Extraction scheme B). This process solubilized 84% of the activity. After neutralization and evaporation, the residue was sonicated with ethanol and filtered. The ethanol soluble portion (12% total activity) was subjected to TLC and 53% found to be HOE 54014 with 47% at the origin. Therefore, 6.4% of the rice leaf residue (0.53 X 12%) consisted of components hydrolyzable to the benzoxazolone HOE 54014. The remainder of the acid solubilized activity (72% total label) that did go into ethanol was mixed with water and filtered. Forty-eight percent went into the water (leaving presumably, 24% acid soluble but not ethanol or neutral aqueous soluble). That 48% remained at the TLC origin and was thus designated as "unidentified highly polar compounds".

The results of the two extraction schemes are in good agreement in the sense that 4% and 6.4% of the radiolabel was found as compounds that could be hydrolyzed to HOE 54014 as in the analytical method. The soybean study found a much higher proportion of the residue (43%) could be measured in this way. Also, most (79%) of the soybean residue was extracted by ether and methylene chloride/water without the need for an acid reflux. We believe the difference between the trials is due to the time allowed to pass between application and harvest (15 days for soybeans, 83 days for rice). It is likely that the longer PHI for rice leaves permitted more extensive degradation to highly polar products and/or reincorporation into natural plant components."

Two metabolism studies on rice (Hoechst Reports No. A30298 and A30296) are submitted with PP#6F3316 (Accession No. 073956, Tabs D-8 and D-9).

A field study was conducted to supplement a greenhouse study and to determine the nature of polar residues in rice. <sup>14</sup>C-chlorophenyl-labeled fenoxaprop-ethyl was applied to rice at the 5 to 6 leaf stage at the rate of 0.11 kg ai/ha (0.1 lb ai/A). The radioactivity in the plant parts was determined by liquid scintillation counting after combusting aliquots of the solid materials and absorbing the <sup>14</sup>CO<sub>2</sub> in an alkaline solution. Residues in new leaves 22 days after treatment were less than 2 percent of those in leaves treated originally. Residues in new stem growth were approximately 8 percent of those in treated stems. The radioactivity found in rice plant parts is summarized below:

	<u>INTERVAL FROM APPLICATION TO SAMPLING (DAYS)</u>	<u>FENOXAPROP-ETHYL EQUIVALENTS FOUND (PPM)</u>
LEAVES	0	71.0
	22 (direct spray leaves)	6.9
	(direct spray stems)	0.87
	(new growth leaves)	0.11
	(new growth stems)	0.07
	36 (new growth leaves)	0.05
	63 (new growth leaves)	0.017
	106 (new growth leaves)	0.004
STRAW	36 (direct spray straw)	36.4
	63 (direct spray straw)	11.5
	106 (straw 0-35 cm)	0.11
	(new growth straw)	0.038
PANICLES	63	0.005
	106 (stems of panicles)	< 0.002
ROUGH RICE	106	< 0.002

Residues in rice leaves 22 days after treatment were characterized using thin layer chromatography and high performance liquid chromatography. Of the 42.5 percent (declared by the petitioner) of the total radioactive residue which was extractable with acetonitrile/water, the following compounds were characterized:

	<u>Percent of Total Radioactivity in Rice Leaves</u>
HOE 33171	0.5
HOE 53022	3.8
HOE 54014	3.2
HOE 40356	0.2
Unknowns	5.8
Highly polar compounds	12.8
Sum of all compounds which contain the benzoxazol fragment	13.7
Losses during workup	16.2

When the residues remaining in the filter cake after the acetonitrile/water extractions were subjected to acid hydrolysis

and extraction, additional residues amounting to approximately 20 percent of the total radioactivity in rice leaves were identified as HOE 54014. Thus, there is about 28 percent of total accountable radioactivity containing the 6-chlorobenzoxazole moiety from HOE 33171, HOE 53022, and HOE 54014 in rice leaves at 22 days.

Another field study was conducted using  $^{14}\text{C}$ -dioxypyphenyl-labeled fenoxaprop-ethyl. Rice was treated at the 5- to 6-leaf stage at the rate of 0.07 kg ai/ha (0.06 lb ai/A). Residues in new leaves 22 days after treatment were less than 2 percent of those in treated leaves. Residues in new stem growth 22 days after treatment were 59 percent of those in treated stems. The radioactivity found in leaves, stems, straw, and rice is summarized below:

<u>MATRIX</u>	<u>INTERVAL FROM APPLICATION TO SAMPLING (DAYS)</u>	<u>FENOXAPROP-ETHYL EQUIVALENTS FOUND (PPM)</u>
LEAVES AND STEMS	0	32.6
	22 (direct spray leaves)	6.7
	(direct spray stems)	0.22
	(new growth leaves)	0.09
	(new growth stems)	0.13
	36 (new growth leaves)	0.05
	63 (new growth leaves)	0.012
	106 (new growth leaves)	0.002
STRAW	36 (direct spray straw)	19.6
	63 (direct spray straw)	2.9
	106 (straw 0-35 cm)	0.06
	(new growth straw)	0.022
RICE	106	< 0.002

Residues in rice leaves 22 days after treatment were characterized by thin layer chromatography and high performance liquid chromatography. Of the 46.1 percent (declared by the petitioner) of the total radioactive residue which was extractable with acetonitrile/water, the following compounds were characterized:

	<u>Percent of Total Radioactivity in Rice Leaves</u>
HOE 33171	1.2
HOE 53022	12.8
HOE 20686	3.2
HOE 40356	1.3
Unknowns	7.6
Highly polar compounds	12.0
Sum of all compounds which contain the HPP-acid-fragment (hydroxy-phenoxy-propanoic acid fragment)	40.0
Loss during workup	7.8

When the residues remaining in the filter cake after the acetonitrile/water extractions were subjected to acid hydrolysis and extraction, additional residues amounting to 10.1 percent of the total radioactivity in rice leaves were identified as HOE 20686. In this metabolism study, about 14 percent of the total accountable radioactivity contained the 6-chlorobenzoxazole moiety of HOE 33171 and HOE 53022 in rice leaves at a 22-day PHI.

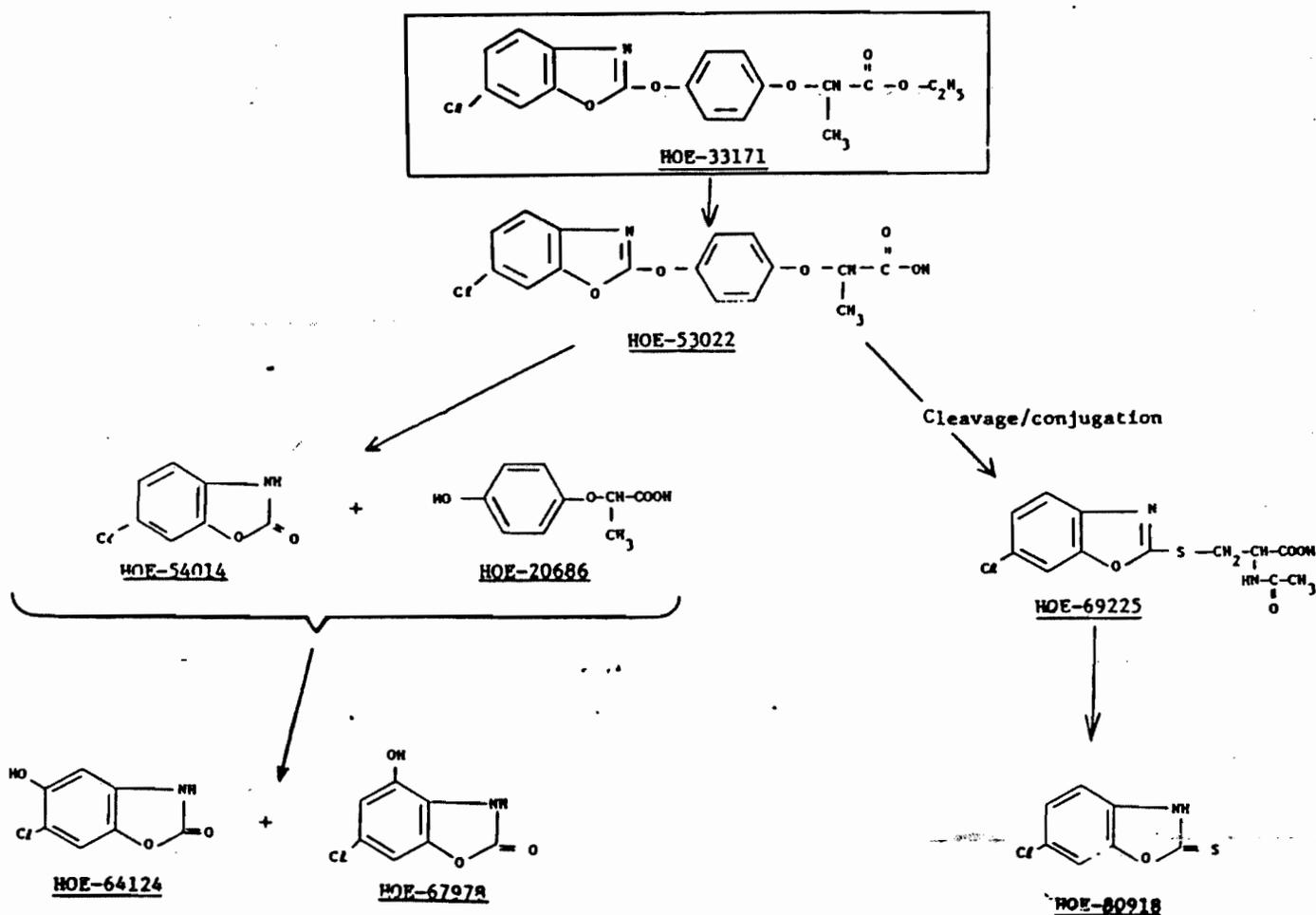
The following chart compares residues of fenoxaprop-ethyl which were determined in rice leaves at a 22-day preharvest interval using a  $^{14}\text{C}$ -chlorophenyl label vs. a  $^{14}\text{C}$ -dioxiphenyl label.

	<u><math>^{14}\text{C}</math>-Chlorophenyl Label</u>	<u><math>^{14}\text{C}</math>-Dioxiphenyl Label</u>
extractable residues	42.5	46.1
HOE 33171	0.5	1.2
HOE 53022	3.8	12.8
HOE 54014	3.2	0.0
HOE 40356	0.2	1.3
HOE 20686	0.0	3.2
unknowns	5.8	7.6
highly polar	12.8	12.0
extractable residues resulting from acid hydrolysis of MARC		
HOE 54014	20.3	0.0
HOE 20686	0.0	10.2

A glossary (Attachment 1) of chemical structures and chemical names for fenoxaprop-ethyl and related compounds is attached to this review.

### Animals

A rat metabolism study (Hoechst Report No. A30491) is submitted. Both  $^{14}\text{C}$ -chlorophenyl-ring labeled HOE 33171 and  $^{14}\text{C}$ -dioxypyphenyl-ring labeled HOE 33171 were used in the study. HOE 33171 is metabolized by the rat as indicated below:



A lactating cow metabolism study is submitted with this petition. A lactating cow was fed 50 mg/day of  $^{14}\text{C}$ -chlorophenyl labeled fenoxaprop-ethyl for 3 days. The cow was sacrificed 24 hours after the last dose. Tissues, milk, and urine were analyzed. Radioactive residues were 0.005 ppm in muscle, 0.020 ppm in subcutaneous fat, 0.11 ppm in liver, and 0.20 ppm in kidney. In milk, residues at 6.5 hours after the first dose were 0.005 ppm fenoxaprop-ethyl equivalents. (The first, second, and third doses were given at 0, 24, and 48 hours.) For milk which was sampled at 23, 30, 47, 54, and 71 hours, residues ranged from 0.036 to 0.062 ppm. Residues in urine (4 to 8 hours after the first dose) were characterized by thin layer chromatography (TLC) to be 64 percent HOE 69225, 9 percent HOE 54014, and 5 percent HOE 80918 in one TLC development system, and 73 percent HOE 69225 and 10 percent HOE 54014 in another TLC development system. Residues in muscle tissue were not characterized due to insufficient residues. Residues in other tissues were analyzed by a method which hydrolyzed residues with acid to form 6-chloro-2,3-dihydrobenzoxazole-2-one (HOE 54014), which is derivatized for GC analysis as 3-acetyl-6-chloro-2,3-dihydrobenzoxazol-2-one. Thirty-two percent of the residues in liver and 23 percent of the residues in kidney were determined by this method to contain the 6-chloro-2,3-dihydrobenzoxazole-2-one moiety. Since approx. one-third of the residue in kidney fat and subcutaneous fat was carried through the analytical procedure, the petitioner determined that <30% of the residues in kidney fat and <25% of the residues in subcutaneous fat contained the 6-chloro-2,3-dihydrobenzoxazole-2-one moiety, although no HOE 54014 was detected by the analytical procedure. 75% of the total radioactivity in milk was determined to contain the 6-chloro-2,3-dihydrobenzoxazol-2-one moiety. (Ten percent of the total radioactivity in milk were unidentified polar compounds which remained in the water phase after separation of the fat phase. Eighty-three percent of the residues in the milk fat phase contained the HOE 54014 moiety).

No poultry metabolism study has been submitted.

#### RCB's Comments/Conclusions on the Metabolism Data

##### Plants

To summarize plant metabolism, identified residues in soybean leaves using  $^{14}\text{C}$ -chlorophenyl-ring-labelled HOE 33171 were 28.7% HOE 33171, 4.7% HOE 53022, 4.2% HOE 67978, 7.3% HOE 64124, and 9.9% HOE 54014, totaling 55% of the total  $^{14}\text{C}$ . Identified residues in soybean leaves using  $^{14}\text{C}$  label in the dioxyphenyl ring of HOE 33171 were 29.2% HOE 33171, 12.2% HOE 53022, 2.3% HOE 20686, and 1.1% HOE 40356, totaling 44.8% of the total  $^{14}\text{C}$ .

Identified residues in rice leaves using the  $^{14}\text{C}$ -chlorophenyl label are 0.5% HOE 33171, 3.8% HOE 53022, 23.5% HOE 54014, and 0.2% HOE 40356, totaling 28% of the  $^{14}\text{C}$ -chlorophenyl label. Identified residues in rice leaves using the C-dioxyphenyl label are 1.2% HOE 33171, 12.8% HOE 53022, 1.3%

HOE 40356, 13.4% HOE 20686, totaling 28.7% of the total <sup>14</sup>C-chlorophenyl label.

Residues that have been identified in plants are HOE 33171, HOE 53022, HOE 67978, HOE 64124, HOE 54014, HOE 20686, and HOE 40356.

The analytical method measures free and conjugated HOE 33171, HOE 53022, and HOE 54014 by hydrolyzing these compounds to HOE 54014.

In a soybean metabolism study, the petitioner has claimed that total radioactive fenoxaprop-ethyl residue in seeds was less than 0.005 ppm (PHI's 51 to 126 days); however, although the proposed analytical method has the capability to analyze about one-third of the terminal residue (after loss), the field studies (discussed later in this review) indicated that more total terminal residue could be present in seeds (see the Residue Section of this review for more details).

RCB defers to TOX as to whether the identification of 55% and 28% of the residues in soybeans and rice, resp., is adequate for TOX considerations.

#### Animals

To summarize animal metabolism, identified residues in rats were HOE 33171, HOE 53022, HOE 54014, HOE 20686, HOE 64124, HOE 67978, HOE 69225, and HOE 80918.

Identified residues in lactating cow urine were 64% HOE 69225, 9% HOE 54014, and 5% HOE 80918 in one TLC development system, and 73% HOE 69225 and 10% HOE 54014 in another TLC development system. Residues, analyzed by a method which hydrolyzed residues with acid to form 6-chloro-2,3-dihydrobenzoxazole-2-one (HOE 54014) indicated that 32% of the residues in liver and 23% of the residues in kidney contained the 6-chloro-2,3-dihydrobenzoxazole-2-one moiety. Less than 30% of the residues in kidney fat and less than 25% of the residues in subcutaneous fat contained the 6-chloro-2,3-dihydrobenzoxazole-2-one moiety. Seventy-five percent of the total radioactivity in milk contained the 6-chloro-2,3-dihydrobenzoxazole-2-one moiety.

Identified residues in animals are HOE 33171, HOE 53022, HOE 54014, HOE 20686, HOE 64124, HOE 67978, HOE 69225, and HOE 80918.

#### Plants and Animals

Of the identified residues, HOE 33171, HOE 53022, HOE 67978, HOE 64124, HOE 54014, and HOE 20686 are found in both plants and animals. HOE 40356 has been identified in plants but not in animals; HOE 69225 and HOE 80918 have been identified in animals but not in plants.

Although, the petitioner has made an effort towards understanding the metabolism of fenoxaprop-ethyl in soybeans, rice, and the lactating cow, RCB reserves any final conclusions until TOX has had a chance to comment on this issue. If TOX feels

that further identification of residues is needed for toxicological considerations, then the petitioner should do further metabolic work. In order to further identify the nature of the  $^{14}\text{C}$ -activity, the petitioner may want to consider, among various possibilities, the following: exhaustive reflux extraction with HBr or HI instead of HCl; exhaustive extractions with other solvents such as ether, acetone, etc.; enzymatic hydrolysis; column chromatography of polar residues in the water phase by gel permeation chromatography and/or ion-exchange chromatography; and electrophoresis of polar residues in the water phase. The preceding are only some suggestions. The petitioner, of course, will want to use the best available technology in order to provide the necessary metabolism understanding.

### Analytical Methods

#### Plants

The analytical method for plants is American Hoechst Corporation's Method No. AL 3/84. The sample is hydrolyzed in an aqueous alcoholic hydrochloric acid medium under reflux in a Soxhlet apparatus. The residues (parent, HOE 53022) are converted to 6-chloro-2,3-dihydrobenzoxazol-2-one. After filtration and isolation, the 6-chloro-2,3-dihydrobenzoxazole-2-one is acetylated with acetic anhydride and determined as 3-acetyl-6-chloro-2,3-dihydrobenzoxazole-2-one by gas chromatography with an electron capture detector.

Recoveries of fenoxaprop-ethyl residues from soybeans and rice samples fortified at the time of the petitioner's method evaluation are listed below:

<u>Commodity</u>	<u>Fortification Level (ppm)</u>	<u>% Recovery</u>
Soybean seeds	0.05	65-100
	0.10	65-103
	<del>0.50</del>	73-86
Soybean forage	0.02	65-73
	0.05	57-88
	0.10	62-87
	0.50	69-77
	1.00	71
Soybean straw	0.05	96
	0.10	117
Soybean hulls	0.05	72-116
	0.10	74
Soybean meal	0.02	42-43
	0.05	35-78

<u>Commodity</u>	<u>Fortification Level (ppm)</u>	<u>% Recovery</u>
Soybean oil	0.02	61
	0.05	46-73
	0.10	86
Soybean soapstock	0.10	75
Rice grain	0.02	59-106
	0.05	70-115
	0.10	85-128
Rice straw	0.02	66-124
	0.05	73-114
	0.10	72-112
Rice forage	0.02	96-105
	0.05	70-101
	0.10	119
	1.00	59
	5.00	74
Rice bran	0.02	63-113
	0.05	71-113
Rice hulls	0.02	53
	0.05	76
	0.10	95
Milled rice	0.02	53-115
	0.05	77-107
	0.10	84-90

The above fortified recoveries of fenoxaprop for soybean seeds, rice grain, and rice straw were determined during the residue analysis process. Recoveries for HOE 33171 and its metabolites HOE 54014 and HOE 53022 from soybean seeds, rice grain, and rice straw were determined in a separate recovery study as follows:

<u>MATRIX</u>	<u>COMPOUND</u>	<u>FORTIFICATION LEVEL (PPM)</u>	<u>PERCENT RECOVERY</u>
Rice Grain	HOE 33171	0.02	100
		0.05	85
		0.10	100
	HOE 54014	0.02	139
		0.05	106
		0.10	86
	HOE 53022	0.02	101
		0.05	101
		0.10	97

<u>MATRIX</u>	<u>COMPOUND</u>	<u>FORTIFICATION LEVEL (PPM)</u>	<u>PERCENT RECOVERY</u>
Rice Straw	HOE 33171	0.02	112
		0.05	77
		0.10	109
	HOE 54014	0.02	96
		0.05	103
		0.10	106
	HOE 53022	0.02	97
		0.05	87
		0.10	84
Soybean Seed	HOE 33171	0.02	115
		0.05	123
		0.10	90
	HOE 54014	0.02	79
		0.05	85
		0.10	105
	HOE 53022	0.02	74
		0.05	101
		0.10	63

The claimed limit of determination of the method for soybeans and rice is 0.05 ppm.

#### Animals

The analytical method for animals is American Hoechst Corporation's Method No. AL 6/84. The sample is hydrolyzed with hydrochloric acid in acetonitrile under reflux to convert the residues to 6-chloro-2,3-dihydrobenzoxazole-2-one. After filtration, the active ingredient is isolated on an Extrelut column. The 6-chloro-2,3-dihydrobenzoxazole is acetylated with acetic anhydride and determined as 3-acetyl-6-chloro-2,3-dihydrobenzoxazole-2-one by gas chromatography with an electron capture detector.

The petitioner states that recoveries at fortification levels of 0.02 to 0.5 ppm were 75 to 90 percent. The petitioner also states that the limit of determination of the method is 0.02 ppm.

The specificity of the analytical method AL 6/84 was determined by checking the following pesticides for interference: Acephate, Alachlor, Azinphosmethyl, Barban, Bentazon, Bifenox, Blazer, Carbaryl, Carbofuran, Chloramben, Chlorpropham, Chlorpyrifos, Cyanazine, Dalapon, 2,4-DB-Acid, DCPA, Diclofop-methyl, Diflufenzuron, Dimethoate, Dinoseb, Diphenamid, Diuron, DSMA, EPN, EPTC, Fluchloralin, Fluometuron, Glyphosate, Harvade, Linuron, Mefluidide, Methamidophos, Methidathion, Methomyl, Methoxychlor,

Methoxychlor P,P', Monocrotophos, Norflurazon, Oryzalin, Oxyfluorfen, Paraquat dichloride, Parathion-methyl, Pendimethalin, Permethrin-Mix, Phosmet, Prometryn, Propachlor, Thidiazuron, Trifluralin, and Vernolate. The petitioner states that no interference from the other pesticides was observed in the determination of fenoxaprop-ethyl.

RCB's Comments and Conclusions on the Proposed Analytical Methodology Submitted for Regulatory Purposes

RCB previously reviewed a plant analytical method using gas chromatography-mass spectroscopy with monitoring of the m/e 169 peak in connection with the EUP on soybeans (PP#3G2940, R. Loranger, 11/9/83), and a plant analytical method using gas chromatography-electron capture detection in the EUP on rice (PP#4G3035, R. Loranger, 6/7/84).

In principle, residues in the plant samples are extracted in an alcoholic hydrochloric acid medium, and residues in animal tissues are extracted in an acetonitrile - hydrochloric acid medium. The petitioner uses hydrochloric acid as a cleaving agent with the intent of converting the parent compound and the metabolite HOE 53022 to HOE 54014 (6-chloro-2,3-dihydrobenzoxazol-2-one) which is also one of the metabolites that was defined. But, is HCl the right choice of acid for cleaving the preceding compounds? One notices that etheral bonds (-O-) are located at two positions in HOE 33171 and HOE 53022. According to March (Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, p. 344, McGraw-Hill, New York, 1968) the following is stated:

"Ethers may be cleaved by heating with concentrated HI or HBr. HCl is seldom successful. HBr reacts more slowly than HI, but it is often a superior reagent, since it causes fewer side reactions."

At this time, RCB will reserve its conclusion on the acceptance of the proposed analytical methodology for regulatory purposes until RCB has received an answer to its deference to TOX concerning the adequacy of the characterization of residues for toxicological consideration and/or the nature of the residue in plants and animals is finalized. More work may need to be done on the proposed analytical methodology.

RCB has requested (January 8, 1986 telephone conversation between N. Dodd - EPA and William Horton - American Hoechst Corp.) the petitioner to submit the metabolic standards HOE 53022 and HOE 54014 to its North Carolina depository in preparation for an EPA method trial. Although the analytical procedure is questionable, RCB will submit it for a method trial. After TOX has answered RCB's deference concerning the toxicological significance of the residue and work has been finalized on the proposed regulatory procedure, a final determination will be made as to what residues need to be regulated.

The identity of HOE S 1728 (ATA TH-T of the Hoechst Company), which is an emulsifier solution used in the analytical method, is needed.

Residue DataStorage Stability

Storage stability of fenoxaprop-ethyl in soybean seeds fortified at 1.0 ppm and stored at -20 °C for a 2-year period was determined. Recoveries on days 0, 193, 507, and 695 for soybean seeds were 83 percent, 87 percent, 116 percent, and 107 percent, respectively.

All soybean and rice samples submitted with this petition were stored for 2 years or less.

RCB concludes that adequate storage stability data are available for the parent compound fenoxaprop-ethyl only. However, since it appears that fenoxaprop-ethyl is highly systemic and much more of the metabolites are present in the terminal residues of weathered crops than the parent compound, the petitioner should also submit storage stability data for those major metabolites that will be regulated. At this time, we do not know what these regulative metabolites will be since more metabolic work may need to be done.

Soybeans

Twenty-three studies which were conducted on soybeans in 10 states between 1979 and 1982 were previously reviewed (PP#3G2940, R. Loranger, November 9, 1983). In most of those studies, HOE 33171 was applied 1 to 2 times at the rate of 0.15 to 0.4 lb ai/A with PHI's of 46 to 148 days. In the 1979 studies, residues after one application at the rate of 0.49 to 1.0 lb ai/A with PHI's of 112 to 153 days were also determined. At least 2 studies involved use of crop oil in the spray mixture. Residues were found in samples treated during the bloom stage, such as residues of 0.05 ppm found in soybeans treated twice at the rate of 0.15 lb ai/A with an 86-day PHI. The only samples treated closer than 70 days to harvest contained residues of 0.12 to 0.19 ppm (2X rate of 0.4 lb ai/A) reflecting a 46-day PHI (still bloom stage). [RCB files ("Stages of Soybean Development," Iowa State University, 1977) indicate that the average time from full bloom to maturity ranges from 45 to 70 days.] Residues in soybeans were all < 0.05 ppm for soybeans treated before bloom. (No data were submitted on residues in soybean forage, hay, and straw).

An additional 17 studies on soybeans in the 10 states of IA, IN, LA, WI, NJ, MS, MD, AR, MN, and NE are submitted with this petition. Crop oil concentrate (1 qt) was applied in two studies (LA and AR) with the HOE 33171. In two additional studies (IN and MN), crop oil concentrate (1 pt or 1 qt) was applied with Basagran (which was applied 6 days before or 2 days after the HOE 33171 application). Whip IEC was applied postemergent 1 or 2 times at rates of 0.15, 0.20, or 0.40 lb ai/A (except for one study in which the application rate was 1.0 lb ai/A). The majority of the studies involved ground applications in 20 to 40 gal spray/A. Three studies involved one aerial application at the rate of 0.15

or 0.20 lb ai/A in 5 to 10 gal spray/A. A fourth study involved both a ground and an aerial application at the rate of 0.20 lb ai/A. In 13 studies, only the seed was analyzed (except for 0-day foliage in one study). In a 14th study, seed and straw were analyzed. In the three remaining studies, seed and processing fractions were analyzed. Preharvest intervals for the 17 studies ranged from 60 to 147 days. Residues which were searched for by the analytical method (AL3/84) were combined residues of HOE 33171, HOE 54014, and HOE 53022. No detectable residues (< 0.05 ppm) were found in soybean seeds (in all 17 studies). In the one study in which straw was analyzed, no detectable residues (< 0.05 ppm) were found. In two of the three studies in which processing fractions were determined, no detectable residues (< 0.05 ppm) were found in seed, meal, crude oil, refined oil, and soapstock. In one of the three studies (in which preharvest intervals were 78 days for one application and 66 days for 2 applications), initially reported residues for soybean hulls were 0.04 ppm for 1 treatment at the rate of 0.2 lb ai/A, 0.10 ppm for 2 treatments at the rate of 0.2 lb ai/A, 0.03 ppm for one treatment at the rate of 0.4 lb ai/A, and 0.10 ppm for two treatments at the rate of 0.4 lb ai/A. Upon reanalysis, residues were less than the claimed validated limit of quantitation (0.05 ppm). In the second of the three studies, combined residues of HOE 33171, HOE 54014, and HOE 53022 in hulls were not detectable (< 0.02 ppm) except for residues of 0.02 ppm for two treatments at 0.2 lb ai/A and a 73-day PHI. In the third processing study (in MS), combined residues of HOE 33171, HOE 54014, and HOE 53022 for two treatments at 0.2 lb ai/A and an 86-day PHI were not detectable (< 0.05 ppm) in soybean seeds, not detectable in refined oil, 0.059 ppm in hulls, and 0.051 ppm in meal. Residues for two treatments at 1.0 lb ai/A (5X the proposed application rate) and an 86-day PHI were 0.114 ppm for seed (Note: The average time from full bloom to maturity ranges from 45 to 70 days), 0.094 ppm for hulls, 0.086 ppm for meal, and not detectable for refined oil.

### Rice

Nine studies on rice in the 4 states of TX, LA, AR, and MS were previously reviewed (PP#4G3035, R. Loranger, June 7, 1984). The 0.75 EC formulation was applied at rates of 0.2 and 0.4 lb ai/A in 6.7 to 30 gallons spray per acre. Applications were made at the 2- to 6-leaf stage of the rice crop. Preharvest intervals were 79 to 121 days. The petitioner's residue data indicate that no detectable residues (< 0.02 ppm) were found in grain and straw. In three studies in which rice was processed into hulls, bran, and milled grain, no detectable residues were detected in hulls, bran, and milled grain. Although residues were found in rice shoots on the day of application, RCB determined that these residues were not a problem since the crop will not be used for food or feed at that stage.

An additional 19 studies on rice in the 6 states of TX, MS,

LA, CA, AR, and MO are submitted with this petition. HOE 33171 was tank mixed with Basagran in at least four of the studies. Whip 0.75 EC was applied postemergence once at the rate of 0.10 to 0.40 lb ai/A or twice at the rate of 0.15 lb ai/A (or 0.15 + 0.20 lb ai/A) in 6.7 to 49 gallons spray per acre. At least seven of the studies involved at least one aerial application. Preharvest intervals for grain and straw ranged from 78 to 131 days. Grain was analyzed in 16 of the studies. Only straw was analyzed in three of the studies. Hulls, brans, and milled grain were analyzed in two studies. Foliage was analyzed in three studies. Residues which are claimed to be determined by the analytical method (AL 3/84) are combined residues of HOE 33171, HOE 54014, and HOE 53022. No detectable residues (< 0.02 ppm) are reported in grain and straw except for one study in which residues of 0.03 ppm in straw were found 93 days after one application in CA at the rate of 0.15 lb ai/A plus surfactant. No detectable residues (< 0.02 ppm) were found in hulls, brans, or milled grain. Residues in foliage in one study decreased from 30 ppm at 0-day to 0.03 ppm at 30 days when treated at 0.15 lb ai/A and decreased from 50 ppm at 0 days to < 0.02 ppm at 30 days when treated at ~~0.50 lb ai/A~~. (Only 0-day residues were reported in the other two foliage studies.)

RCB previously indicated (PP#4G3035, R. Loranger, June 7, 1984) that residue data for rice grown in CA should be provided. This requirement is satisfied with the present submission, which includes five residue studies on rice in CA.

RCB also previously concluded (PP#4G3035, R. Loranger, June 7, 1984) that since no residues were detected in rice grain, straw, hulls, bran, or milled grain, no food/feed additive tolerances were needed. In the studies now submitted, the only detectable residue was 0.03 ppm on straw resulting from one application of Whip 0.75 EC with a surfactant. In the same study, no residues were detected in rice straw when no surfactant was used.

#### RCB's Comments/Conclusions on the Field Residue Data

At this time, RCB must reserve its conclusion on the adequacy of the proposed 0.05 ppm fenoxaprop-ethyl tolerance on soybeans and possibly soybean fractions; more work on plant metabolism and methodology may have to be done. The petitioner may argue that he has submitted the results from one soybean metabolism study which indicates that the total radioactive fenoxaprop-ethyl residue in seeds was less than 0.005 ppm (PHI's 51 to 126 days); therefore, it is immaterial that his proposed regulatory procedure is capable of determining at maximum only about one-third of the terminal residue. This 0.005 ppm value is informative with regard to that particular soybean metabolism study, but it does not help in the evaluation of the residue data. Generally, it is found that the results from total radioactive analyses will be moderately higher than those obtained from GLC analyses. Here, this is not the case. Even though the GLC procedure at maximum may only determine about one-third of the terminal residue, it is observed in one of the processing studies that whole soybeans treated at 5X application contain 0.114 ppm fenoxaprop-ethyl residues (PHI = 86 days); this

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translates to 0.023 ppm for 1X application which is about 4.6 times more residue than that 0.005 ppm total residue reported in the soybean metabolism study. Incidentally, although the petitioner has reported all of his residue data as being < 0.05 ppm, he has reported recovery data as low as 0.02 ppm (assumption: samples were fortified at the time of analyses).

In addition to the preceding, the recovery/validation data for fenoxaprop-ethyl in soybeans/soybean fractions could be misleading even though at face value most of them would seem to be acceptable. Why is there some doubt? Since the petitioner's metabolic work indicates that much of the radioactivity was not isolated from the plant substrate wherein substantial accountability of the terminal residue is exemplified, it becomes very difficult to accept validation data for the proposed analytical methodology where standards for the parent compound and its identified metabolites are added to the sample immediately before analyses. Generally, RCB will approve of validation data where the concerned residues necessary for regulation are added to the samples before analyses, but there ~~must be a~~ good correlation between the accountable residues in the metabolism study and the accountable residues in the proposed analytical procedure.

Finally, it is noticed that in one of the "1X application - PHI = 86 days" processing studies < 0.05 ppm fenoxaprop-ethyl was reported for whole soybeans, 0.059 ppm for hulls, and 0.051 ppm for soybean meal. Remember, first of all, that the analytical procedure is claimed to account for about one-third of the terminal residue. And, in addition to this, the recovery/validation data for soybean meal range from 35 percent to 78 percent at the fortification level of 0.05 ppm even when the standards were added to the sample presumably before analyses. Thus, assuming that the analytical methodology is recovering residues at the lower end of the recovery spectrum, it is quite possible that a residue (parent plus two metabolites - HOE 53022 and HOE 54014) near 0.2 ppm instead of 0.051 ppm could actually exist in the soybean meal.

In view of the above, RCB reserves its final conclusion concerning the adequacy of the proposed 0.05 ppm fenoxaprop-ethyl tolerance on soybeans and possibly soybean fractions; more work may have to be done on plant metabolism and the analytical procedure that is proposed for regulatory purposes. The petitioner should be informed that it may be necessary for him to reanalyze some of his reserve field soybean samples as a result of the preceding work. Also, if the storage stability data for the parent and major metabolites are not adequate, then new field residue data may need to be generated.

At this time, RCB reserves its conclusion on the adequacy of the proposed 0.05 ppm fenoxaprop-ethyl tolerance on rice grain and straw (rice straw and hulls may be fed to livestock).

The petitioner reports all of his residue values for rice grain, straw, and rice fractions as < 0.02 ppm except for one value of 0.03 ppm on straw under the field residue discussion (PHI's are 79 to 121 days). However, when looking at the field radioactive rice metabolism studies, it seems that harvested straw would particularly have undisputable levels of finite residues. For example, in one study, fenoxaprop-ethyl was applied at a rate of 0.1 lb ai/A which is one-fourth of the overall proposed use of 0.4 lb ai/A/season. At 106 days after application, the straw 0 to 35 cm high contained 0.11 ppm fenoxaprop-ethyl equivalents and the new growth straw 0.038 ppm. Multiplying each of these two values by 4, then theoretically, the straw 0 to 35 cm high could contain about 0.44 ppm fenoxaprop-ethyl equivalents and the new growth straw 0.15 ppm. Incidentally, when setting a tolerance on straw, it is impractical to consider separately the residues on different lengths of the stem, that is to say, the whole stem should be considered and analyzed for residues.

In view of the above, RCB reserves its final conclusion concerning the adequacy of the proposed 0.05 ppm fenoxaprop-ethyl tolerance on rice grain and straw; more work may have to be done on the plant metabolism and the proposed analytical procedure for regulatory purposes. The petitioner should be informed that it may be necessary to reanalyze some of his reserve field rice samples as a result of the preceding work; the storage stability study on the parent compound and the major metabolites must be adequate in order to accept these data from reanalyses. Otherwise, it may be necessary to generate some new field residue data.

#### Meat, Milk, Poultry, and Eggs

No cattle or poultry feeding studies have been submitted. Soybeans, soybean hulls, rice straw, and hulls may be fed to livestock.

RCB must reserve its conclusion on the immediate need for cattle and poultry feeding studies until those questions relating to the plant metabolism, proposed analytical methodology, and field residue studies have been considered adequate.

#### Other Considerations

An International Residue Limits (IRL) Status Sheet is attached. There are no Codex, Canadian, and Mexican tolerances for fenoxaprop-ethyl on soybeans and rice. Therefore, no compatibility questions exist with respect to Codex.

Attachment 1: Glossary

Attachment 2: International Residue Limit Status Sheet

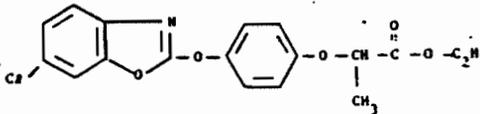
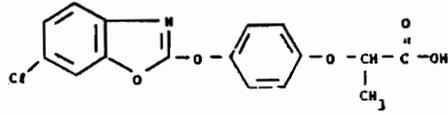
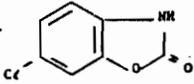
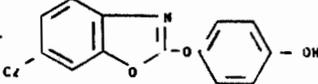
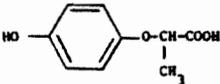
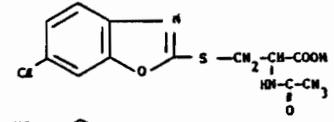
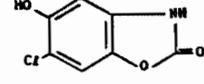
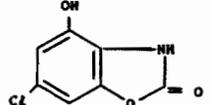
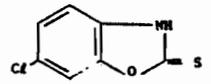
Attachment 3: Confidential Appendix

cc (with Attachments 1, 2, and 3 only): TOX, Reviewer-N. Dodd, RF, PM #23, PP#6F3316, PMSD/ISB - Eldredge

cc (with Attachments 1 and 2): Circu, EAB, EEB, FDA, D.Marlow  
RDI:J.H. Onley:1/13/86:R.D. Schmitt:1/13/86

TS-769:RCB:CM #2:RM 810:557-1681:N. Dodd:Kendrick & Co:1/16/86

GLOSSARY

<u>Hoechst Code</u>	<u>Chemical Name</u>	<u>Chemical Structure</u>
HOE-33171	ethyl-2-(4-(6-chloro-2-benzoxazolylloxy)phenoxy)propanoate	
HOE-53022	2-(4-(6-chloro-2-benzoxazolylloxy)phenoxy)propionic acid	
HOE-54014	6-chloro-2,3-dihydrobenzoxazol-2-one	
HOE-40356	4-(6-chloro-2-benzoxazolylloxy)phenol	
HOE-20686	2-(4-hydroxyphenoxy)propionic acid	
HOE-69225	6-chloro-benzoxazol-2-mercapturic acid	
HOE-64124	6-chloro-5-hydroxy-2,3-dihydrobenzoxazol-2-one	
HOE-67978	6-chloro-4-hydroxy-2,3-dihydrobenzoxazol-2-one	
HOE-80918	6-chloro-2,3-dihydrobenzoxazol-2-thione	

CHEMICAL Fenoxaprop-ethyl

PETITION NO 6F3316

CCPR NO. \_\_\_\_\_

A Does  
T 1/2/86

Codex Status

Proposed U. S. Tolerances

No Codex Proposal  
Step 6 or above

Residue (if Step 9): \_\_\_\_\_

Residue: Fenoxaprop-ethyl and  
its metabolites\*

Crop(s) Limit (mg/kg)

<u>Crop(s)</u>	<u>Tol. (ppm)</u>
soybeans	0.05
rice	0.05
rice straw	0.05

CANADIAN LIMIT

MEXICAN TOLERANCIA

Residue: \_\_\_\_\_

Residue: \_\_\_\_\_

Crop Limit (ppm)

Crop Tolerancia (ppm)

None

None

Notes:

\* fenoxaprop-ethyl [(±)-ethyl 2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]propanoate] and its metabolites  
2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]propanoic acid and 6-chloro-2,3-dihydrobenzoxazol-2-one,

Fenoxaprop-ethyl scientific review

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Page \_\_\_\_\_ is not included in this copy.

Pages 30 through 32 are not included in this copy.

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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 product 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.

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