UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: February 25, 1998

SUBJECT: **PP#5F4545 and PP#6E4652 QUIZALOFOP-P-ETHYL**. PETITIONS FOR TOLERANCES FOR CANOLA AND MINT.

DP Barcodes: D236729 and D243535 Caswell#: 215D
PRAT Case#: 286774 and Chemical#: 128711
40 CFR: 180.441 Class: Herbicide

TO: Hoyt Jamerson, PM Team 5
MUIREB, RD (7505C)

and

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FROM: S. Knizner and A. Levy
RAB2/HED (7509C)

THRU: Richard Loranger, Branch Senior Scientist
RAB2/HED (7509C)

I. BACKGROUND

E.I. duPont de Nemours and Company, Agricultural Products, the registrant and petitioner, in a letter dated May 23, 1996, submitted an amendment to PP#5F4545 proposing revised tolerances for only canola seed and canola meal (legume vegetable crop group was dropped from the petition). This amendment was submitted in response to deficiencies noted in a previous HED review (see Attachment 1, memo of F. Griffith, 2/21/96, PP#5F4545). The registrant proposed tolerances for the combined residues of the herbicide quizalofop-p ethyl ester (ethyl(R)-2-[4-((6-chloroquinoxalin-2-yl)oxy)phenoxy] propionate), and its acid metabolite quizalofop-p [(R)-2-[4-((6-chloroquinoxalin-2-yl)oxy)phenoxy] propionate) and the S enantiomers of the ester and the acid, all expressed as quizalofop-p ethyl ester, in or on canola seed at 1.0 ppm and canola meal at 1.5 ppm. HED has previously concluded that there are no more residue chemistry

deficiencies relating to this tolerance petition (see Attachment 2, memo of F. Griffith, 6/14/96, PP#5F4545).

IR-4, on behalf of the Oregon Agricultural Experiment Station, petitions for the establishment of a tolerance for the combined residues of the herbicide quizalofop-p ethyl ester (ethyl(R)-2-[4-((6-chloroquinoxalin-2-yl)oxy)phenoxy] propionate), and its acid metabolite quizalofop-p [(R)-2-[4-((6-chloroquinoxalin-2-yl)oxy)phenoxy] propionate), and the S enantiomers of the ester and the acid, all expressed as quizalofop-p ethyl ester, in or on the raw agricultural commodity mint at 3 ppm (PP#6E4652). HED has previously concluded that provided the tolerance level for peppermint, tops and spearmint, tops be established at 2.0 ppm, there are no residue chemistry deficiencies associated with this petition (see Attachment 3, memo of S.Knizner, 5/14/96, PP#6E4652).

II. EXECUTIVE SUMMARY

On October 14, 1997, the Health Effects Division's Hazard Identification Review Committee met to evaluate the toxicology data base of quizalofop-p-ethyl. The toxicology database for quizalofop-p-ethyl is complete. No acute dietary or short-, intermediate-, or chronic-term dermal or inhalation toxicity endpoints were identified. A carcinogenic risk assessment for quizalofop-p-ethyl is not required. The chronic dietary endpoint for quizalofop-p-ethyl comes from the combined chronic toxicity/carcinogenicity study in rats and is based on the occurrence of generalized hepatocyte enlargement in female rats and red blood cell destruction in males at 3.6 mg/kg/day (LOEL). The NOEL in this study was 0.9 mg/kg/day and, using an uncertainty factor of 100, the RfD was 0.009 mg/kg/day.

The Committee determined that an uncertainty factor (UF) of 100 is adequate because: developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits; a two generation reproductive toxicity study in rats showed no increased sensitivity in pups as compared to adults; and the toxicology data base is complete and there are no data gaps.

There are no residential uses for quizalofop-p-ethyl.

Chronic dietary exposure estimates for quizalofop-p-ethyl do not exceed HED’s level of concern. The most highly exposed population subgroup was non-nursing infants less than one-year old at 19% of the RfD. In conducting this chronic dietary risk assessment, HED has made very conservative assumptions -- 100% of mint and canola seed and all other commodities having quizalofop-ethyl tolerances will contain quizalofop-ethyl regulable residues and those residues will be at the level of the tolerance -- which result in an overestimation of human dietary exposure. HED’s drinking water level of concern for infants and children is 73 ppb. Provided EFED estimates of quizalofop-p-ethyl chronic residues in drinking water are less than 73 ppb, aggregate (food, water, and residential) chronic exposure for infants, children, and adults will not exceed HED’s level of concern. HED would

then have no objections to establishment of tolerances for canola and mint as follows:

for the combined residues of the herbicide quizalofop-p ethyl ester (ethyl(R)-2-[4-((6-chloroquinoxalin-2-yl)oxy)phenoxy] propionate), and its acid metabolite quizalofop-p [(R)-2-[4-((6-chloroquinoxalin-2-yl)oxy)phenoxy] propionate) and the S enantiomers of the ester and the acid, all expressed as quizalofop-p ethyl ester, in or on:

canola, seed at 1.0 ppm
canola, meal at 1.5 ppm
peppermint, tops at 2.0 ppm
spearmint, tops at 2.0 ppm

Because no toxicological endpoints have been identified for short-, intermediate-, and/or chronic-term dermal or inhalation exposures, an occupational risk assessment is not required.

III. SCIENCE ASSESSMENT

A. Physical and Chemical Properties Assessment

1. Identification of Active Ingredient

HED has previously concluded that after reviewing the results of the preliminary analysis of the technical grade active ingredient (TGAI) as presented on the Confidential Statement of Formula (CSF) the impurities present in the TGAI quizalofop-p-ethyl are not expected to present a residue problem when formulated into Assure® II and used as directed (F. Griffith, 2/21/96, PP#5F4545).

B. Human Risk Assessment

1. Hazard Assessment

a. Acute Toxicity

Acute toxicity for technical quizalofop-p-ethyl and Assure II are summarized in Tables 1.a. and 1.b.

Table 1.a. Acute toxicity for Technical Quizalofop-p-ethyl (90%).

Guideline No.	Study Type	MRIDs #	Results	Toxicity Category
81-1	Acute Oral - Rat	00073530	LD_{50} = 1670 mg/kg (M) 1480 mg/kg (F)	III
81-2	Acute Dermal - Rat	00073530	LD_{50} = > 5000 mg/kg	IV
81-3	Acute Inhalation	00073530	LC_{50} = 4.8-5.8 mg/L	IV
81-4	Primary Eye Irritation	00073530	Not an irritant	IV
81-5	Primary Skin Irritation	00073530	Negative	IV
81-6	Dermal Sensitization	00073530	Non-sensitizer	NA

Table 1.b. Acute toxicity for Assure II (Quizalofop-p-ethyl 10.3%).

Guideline No.	Study Type	MRIDs #	Results	Toxicity Category
81-1	Acute Oral - Rat	41206111	LD_{50} = 5900 mg/kg (M) 4440 mg/kg (F)	III
81-2	Acute Dermal - Rat	41206112	LD_{50} = > 2000 mg/kg	III
81-3	Acute Inhalation	41206113	LC_{50} = 2.6 mg/L (M) 4.4 mg/L (F)	IV
81-4	Primary Eye Irritation	41206114	Not complete reversibility of effects - severe eye irritant	I
81-5	Primary Skin Irritation	41206115	Slight irritation	IV
81-6	Dermal Sensitization	42147401	Non-sensitizer	NA

In conjunction with the evaluation of PP#5F4545, W. Phang (2/26/96) summarized toxicological data available for quizalofop-p-ethyl. A summary table of studies is included below as Table 2. A detailed discussion of the reproductive and developmental toxicity studies and other studies used for risk assessment endpoints can be found under Dose Response Assessment (2.a.) below. There are no data gaps in the toxicology database.

Table 2. Summary of Toxicological studies for quizalofop-ethyl.

Guideline No.	Study Type	MRIDs #	Results	Effect
82-1(a)	3-month feeding Rat	00250072	NOEL = 40 ppm (2 mg/kg/d) LOEL = 128 ppm (6.4 mg/kg/d)	Increased liver weight and liver lesions
82-1 (a)	3 month feeding - mice	00250073	NOEL < 100 ppm (LDT) (14.3 mg/kg/d)	Liver changes at all doses
82-2	21-Day dermal - rabbit	00073530	NOEL > 2000 mg/kg (HDT)	No dermal or systemic toxicity.
83-1(a)	2-year feeding study - rat	00073531-00073535	NOEL = 25 ppm (0.9 mg/kg/d). LOEL = 100 ppm (3.6 mg/kg/d)	RBC destruction in males. Hepatocyte enlargement in females. See discussion under Dose Response. RfD based on this study.
83-1(b)	1-year feeding study - dog	00073536	NOEL>400 ppm (HDT) (10 mg/kg/d)	
83-2 (b)	Oncogenic 18 month - mice	00255982	Doses tested 0, 2, 10, 80, and 320 ppm. Oncogenic NOEL =80 ppm (11.4 mg/kg/d), LOEL =320 ppm (45.7 mg/kg/d). Systemic NOEL = 10 ppm (1.4 mg/kg/d), LOEL =80 ppm (increased testicular atrophy, enlarged livers, diffuse hepatocyte enlargement). At 320 ppm increased male mortality.	Marginal increase in the incidence of liver tumor in male mice at the highest dose (320 ppm) which exceeded an MTD level (See discussion of carcinogenic Classification under Dose Response section below)
84-4	Mutagenic	00250071 41206108	Unscheduled DNA synthesis Chromosomal Aberration (CHO) Gene mutation (Ames assay) Salmonella	Negative (conc. $1x10^{-5}$ to 6.0 mM) Negative Negative (with/without s9, conc 0.05-50,00ug/pl) All results negative 1)recombinant assays 2) reversion assay
85-1	Metabolism - rat	00073546		Extensively metabolized to the acid form of the test material

2. Dose Response Assessment

On October 14, 1997, the Health Effects Division's Hazard Identification Review Committee met to evaluate the toxicology data base of quizalofop-p-ethyl with special reference to the reproductive, developmental and neurotoxicity data. These data were re-reviewed specifically to address the sensitivity of infants and children from exposure to quizalofop-p-ethyl as required by the Food Quality Protection Act (FQPA). In addition, the Committee also re-assessed the doses and endpoints selected for acute dietary, chronic dietary (RfD), and occupational and residential exposure risk assessments.

a. Uncertainty / Safety Factor

The oral perinatal and prenatal data demonstrated no indication of increased sensitivity of rats or rabbits to *in utero* exposure to quizalofop-p ethyl.

Developmental Toxicity - Rats

In a prenatal developmental toxicity study in rats (unspecified strain) quizalofop ethyl was administered at doses of 0, 30, 100, or 300 mg/kg/day by gavage in 2 mL/kg of 0.5% carboxy-methylcellulose on gestation days 6-15. The study was conducted in two segments, with one segment killed on gestation day 21, and the other allowed to deliver. Functional testing was performed on delivered offspring. For maternal toxicity, the NOEL was 30 mg/kg/day and the LOEL was 100 mg/kg/day based on decreased body weight and food consumption, increased liver weight, and decreased corpora lutea (sic). There were no developmental effects observed. For developmental toxicity, the NOEL was $\geq$ 300 mg/kg/day. **Note: The DER for this study is inadequate; further description of the functional testing is needed, and data should be included in the DER** (MRID 00128206).

Developmental Toxicity - Rabbits

A prenatal developmental toxicity study was conducted in pregnant New Zealand White rabbits (16/group), in which quizalofop ethyl was administered by gavage at doses of 0, 7, 20, or 60 mg/kg/day in 5 ml/kg aqueous 0.5% carboxymethylcellulose and Tween 80 on gestation days 7-19. For maternal toxicity, the NOEL was 20 mg/kg/day and the LOEL was 60 mg/kg/day based on decreased body weight and food consumption. There were no developmental effects observed . For developmental toxicity, the NOEL was $\geq$ 60 mg/kg/day (MRID 40370502).

Reproductive Toxicity - Rats

In a two-generation reproductive toxicity study, Sprague-Dawley rats were fed diets containing quizalofop-p-ethyl at 0, 25, 100, or 400 ppm (0, 1.25, 5.0, or 20 mg/kg/day respectively). The parental NOEL was 100 ppm (5.0 mg/kg/day) and the LOEL was 400 ppm (20 mg/kg/day), based on decreased body weights in males of both generations. The developmental NOEL for effects on the offspring was 25 ppm (1.25 mg/kg/day) and the offspring developmental LOEL was 100 ppm (5.0 mg/kg/day), based on increased incidence of eosinophilic changes in the livers of F2

weanling. In addition, at 400 ppm (20 mg/kg/day), reductions in litter size, survival, body weights, and spleen weight were seen in offspring (MRID 00153351).

The histopathology data for F2 weanlings in the two-generation reproductive toxicity study suggested an increased sensitivity to the offspring. In that study, an increase in the incidence of eosinophilic changes in the liver were noted in the F2 weanlings, and the offspring NOEL was less than the parental systemic NOEL. However, the Committee, raised the following concerns regarding the significance of these observations in the two-generation reproductive toxicity study: 1) the changes in the weanling livers were not well characterized; 2) the biological significance of this endpoint was not known; 3) the precise dose of test substance to 21-day old weanlings cannot be determined with any accuracy, but it is likely to exceed that of the adults; 4) this endpoint (eosinophilic changes), in adults, would not be considered appropriate for use in regulation of a chemical because of the questionable biological significance of this effect; and, 5) liver has been shown to be the target organ in both adults and pups.

For these reasons, the Committee determined that the apparent increase in offspring sensitivity did not justify the retention of an additional uncertainty factor for infants and children.

Summary

The Committee determined that an uncertainty factor (UF) of 100 is adequate because:

(I) Developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits.

(ii) A two generation reproductive toxicity study in rats showed no increased sensitivity in pups as compared to adults.

(iii) The toxicology data base is complete and there are no data gaps.

B. Summary of Toxicological Endpoints for Use in Human Risk Assessment

1) Acute Dietary

Study Selected: None

MRID No.: None

Executive Summary: None

Dose/Endpoint for Risk Assessment: Not Applicable

Comments about Study/Endpoint There were no effects observed in oral toxicity studies that could be attributable to a single dose (exposure). Therefore, a dose and an endpoint have not been identified for this risk assessment.

This risk assessment is NOT required.

2) Chronic Dietary

The RfD was established in 1988:

Study Selected: Combined Chronic Toxicity/Carcinogenicity -Rat (§83-5)

MRID No.: 00073531-00073535

Executive Summary: Groups of male and female Sprague-Dawley rats (50/sex/dose) were fed diets containing quizalofop-p-ethyl at 0, 25, 100 or 400 ppm for 104 weeks. For chronic toxicity, the NOEL was 25 ppm and the LOEL was 100 ppm based on the occurrence of generalized hepatocyte enlargement in female rats and red blood cell destruction in males. In addition, there was generalized hepatocyte enlargement and red blood cell destruction in both sexes at 400 ppm.

Dose/Endpoint for establishing the RfD: NOEL = 25 ppm (0.9 mg/kg/day) based on the occurrence of generalized hepatocyte enlargement in females rats and red blood cell destruction in males at 100 ppm (LOEL).

$$\text{RfD} = \frac{0.9 \text{ mg/kg/day (NOEL)}}{100 \text{ (UF)}} = 0.009 \text{ mg/kg/day}$$

3) Carcinogenic Classification and Risk Quantification

The results of a Second Peer Review Meeting for quizalofop-p-ethyl were summarized in a memo from J. Quest dated 9/9/87. The Peer Review Committee classified quizalofop-p-ethyl as a Category C carcinogen. The memo stated that, 'Because the overall evidence for the oncogenicity of Assure [quizalofop-ethyl] was considered to be weak, it was further recommended that no quantitative risk assessment be performed for the chemical.'

The Science Advisory Panel (SAP) in its meeting on 12/15/87 completed a review of the Agency's peer review classification of

quizalofop-ethyl as a Group C carcinogen. The results of this meeting are contained in a memo by S. Johnson, dated 12/23/87. The Panel's response was as follows,

> "The Panel believes that weight of the evidence does not support classification of Assure [quizalofop-ethyl] in Category C. With the exceptions of an increase in male mouse liver tumors at a dose exceeding the MTD [maximum tolerated dose], all data support classification in Category E. Furthermore, even if the high dose liver tumor data is accepted, the Panel believes that greater statistical rigor is needed to determine significance for variable tumor endpoints such as male mouse liver."

In light of the results of the SAP meeting, the Peer Review Committee met once again on 1/13/88 to reevaluate the carcinogenicity classification for quizalofop-ethyl (see memo of J.Quest, 3/17/88). The results of this meeting are as follows,

> "The Committee concluded that Assure would probably be best categorized in Category D carcinogen (not classifiable as to human carcinogenicity), because limitations in the data from an adequately performed mouse study precluded an accurate interpretation of oncogenic risk. No new animal studies are required. As noted above, this classification of Assure as a Category D oncogen differs from the recommendation of the SAP to place Assure in Category E, due to the presence of the marginal but evident liver tumor response that was observed in the male CD-1 mice."

4) Dermal Absorption

The results of a dermal absorption study in rats indicated that with a 10-hour exposure at doses of 0.19, 1.9 or 19 mg/rat, the percent of absorption was 8.38, 3.27 and 2.9% of the applied dose, respectively (MRID No. 00075546). A dermal absorption factor is not applicable since dermal risk assessments are not required.

5) Short- and Intermediate-Term (Dermal and Inhalation) Occupational and Residential Endpoints

Study Selected: None

MRID No.: None

Executive Summary: None

Dose/Endpoint for Risk Assessment: Not Applicable

Comments about Study/Endpoint: In a 21-day dermal toxicity study, New Zealand White rabbits (5/sex/dose) received 15 repeated dermal applications (aqueous paste) of quizalofop-p-ethyl at doses of 0, 125, 600 or 2000 mg/kg/day, 6 hours/day, 5 days/week over a 21-day period. There was no dermal or systemic toxicity. The NOEL was 2000 mg/kg/day (MRID No. 00073530). In

addition, no maternal or developmental toxicity was observed following *in utero* exposures in rats and rabbits.

These risk assessments are NOT required.

6) Chronic (Dermal and Inhalation) Occupational and Residential (Non-Cancer) Endpoints

Study Selected: None

MRID No None

Executive Summary: None

Dose/Endpoint for Risk Assessment: Not Applicable

Comments about Study/Endpoint: In a 21-day dermal toxicity study, New Zealand White rabbits (5/sex/dose) received 15 repeated dermal applications (aqueous paste) of quizalofop-p-ethyl at doses of 0, 125, 600 or 2000 mg/kg/day, 6 hours/day, 5 days/week over a 21-day period. There was no dermal or systemic toxicity. The NOEL was 2000 mg/kg/day (MRID No. 00073530). In addition, no maternal or developmental toxicity was observed following *in utero* exposures in rats and rabbits.

This risk assessment is NOT required.

TABLE 3. Summary of Toxicological Endpoints for Use in Human Risk Assessment

Exposure Duration	Exposure Route	Endpoint		Comments
		Dose	Effect	
Acute Short-, Intermediate, and Chronic-Term Occupational/ Residential (Dermal and Inhalation)	Dietary Dermal and Inhalation	NA	NA	Risk assessment not required.
Chronic Dietary	Dietary	RfD = 0.009 mg/kg/ d	Hepatocyte enlargement and RBC destruction	
Cancer		Category D		Risk assessment not required.

3. Exposure and Risk Assessment/Characterization

a. Occupational Exposure and Risk Assessment/Characterization

Because no toxicological endpoints have been identified for short-, intermediate-, and/or chronic-term dermal or inhalation exposures, a risk assessment is not required.

Acute data for this formulation are available to HED. Based on the toxicity categories, the work clothing and personal protective equipment (PPE) appearing on the label are in compliance with the Worker Protection Standard (WPS). The label for Assure II lists the following PPE for all handlers: long-sleeved shirt, long pants, chemical-resistant gloves (such as barrier laminate or Viton), shoes plus socks, and protective eyewear.

Acute toxicological data for the technical are available. The Assure II label lists an restricted entry interval (REI) of 12 hours. Based on the toxicity categories for the technical, the 12 hour REI is in compliance with the WPS.

b. Residential and Other Non-Occupational Exposures and Risks

According to a search of REFS on 2/5/98, quizalofop-p-ethyl is not registered for either indoor or outdoor residential uses.

Also, because no toxicological endpoints have been identified for short- and/or intermediate-term dermal or inhalation exposures, this risk assessment is not required.

c. Dietary Exposure and Risk Assessment/Characterization

1) Exposure from Food Sources

(a) GLN 860.1200: Directions for Use

CANOLA

HED has previously concluded that the petitioner has proposed an adequate set of directions for use of quizalofop-p-ethyl, formulated as Assure® II, in conjunction with an approved oil concentrate or a non-ionic surfactant on canola (F. Griffith, 2/26/96, PP#5F4545).

Quizalofop-p ethyl is proposed for use as a selective post emergence herbicide to provide control of annual grasses; eg, fox-tails, barnyardgrass, etc., and perennial grasses; eg, quackgrass. The formulation to be used on the crops is Assure® II Herbicide (EPA Reg. No. 352-541) containing quizalofop-p ethyl at 10.3%, or 0.88 lb a.i. per gallon. In ground applications, apply with standard fan or hollow cone nozzles, not with flood type nozzles. Apply in a minimum of 10 to 20 gallons water per acre, and use either an EPA approved crop oil concentrate at a rate of 4 qts per 100 gallons (1%), or a non-ionic surfactant at a rate of 1 qt per 100 gallon (0.25%). For aerial application, apply in a minimum of 5 gallons water per acre.

To control annual and perennial grasses in canola, apply 7 to 12 ozs of Assure® II (0.7 to 1.2 ozs ai quizalofop-p-ethyl) per acre per application once or twice per crop growing season when the grasses are actively growing, usually when they are around 4 inches high. The maximum application in a crop growing season to canola is 18 ozs Assure® II (1.8 ozs ai) with a 60-day PHI.

The petitioner cautions that the cereal grains are "highly sensitive" to Assure II, thus care should be taken to avoid application when drift is likely. Assure II should not be applied through any irrigation system.

MINT

Quizalofop-p-ethyl is proposed for use as a selective post emergence herbicide to provide control of annual grasses; eg, fox-tails, barnyardgrass, etc., and perennial grasses; eg, quackgrass. The formulation to be used on the crops is Assure® II Herbicide (EPA Reg. No. 352-541) containing quizalofop-p-ethyl at 10.3%, or 0.88 lb a.i. per gallon. A maximum of two applications may be made, using ground equipment, at 0.10 to 0.20

lb ai/A/application. Application should commence when weeds are from 2 to 10 inches tall. The maximum seasonal application rate is 0.20 lb ai/A. Do not apply this product within 30 days of harvest. Do not apply through any type of irrigation system. Do not graze animals on green forage or stubble. Do not utilize hay or straw for animal feed or bedding. Use a minimum of 15 gallons of water per acre. Do not exceed 40 gallons of water per acre. Apply with ground equipment. Always include a spray adjuvant (petroleum based at 1.0% v/v or nonionic surfactant at 0.25% v/v).

(b) GLN 860.1300: Nature of the Residue - Plants

HED has previously concluded that the nature of the quizalofop-p ethyl residue in plants is adequately understood based on metabolism studies in cottonseed, potatoes, soybeans, tomatoes and sugarbeets. The residues of concern are quizalofop-p ethyl and its acid metabolite, quizalofop-p, and the S enantiomers of both the ester and the acid, all expressed as quizalofop-p ethyl (F.Griffith, 2/21/96, PP# 5F4545/FAP# 6H5737) (as per 40 CFR 180.441.

(c) GLN 860.1300: Nature of the Residue - Animals

HED has previously concluded that the nature of the quizalofop-p-ethyl residue in livestock is adequately understood (F.Griffith, 2/21/96, PP# 5F4545/FAP# 6H5737). The residues of concern are quizalofop-ethyl, quizalofop-methyl, and quizalofop acid, all expressed as quizalofop-ethyl (as per 40 CFR 180.441(b)).

(d) GLN 860.1340: Residue Analytical Methods

Method I in PAM II (DuPont Method AMR-153-83, rev. 3) is an adequate enforcement method for determination of quizalofop-p-ethyl and related regulated residues.

The analytical methods used to generate data in support of the proposed tolerances are discussed in Attachments 1 and 3. Sufficient data were provided

(e) GLN 860.1380: Storage Stability Data

Storage stability data have been previously submitted for soybeans and cottonseed (high oil content commodities) which show that quizalofop-p-ethyl, the free acid, and phenols 1, 2, and 4 metabolites are stable in frozen storage for at least 5 ½ months. The petitioner submitted additional frozen storage stability data for quizalofop-p-ethyl, its acid and phenol metabolites in cottonseed, beans, peas, sugarbeets, and canola. These frozen storage stability data for quizalofop acid, phenols 2, 3, and 4 in cottonseeds and cotton processed commodities, snap bean pods and "straw," peas and pea forage, sugarbeet roots, and **canola seed** show that residues are stable for up to 3 years. The data are sufficient to support the magnitude of the residue crop field

trial data submitted in this petition where samples were stored under like conditions and for a shorter time. Storage stability data have been previously submitted for soybeans and cottonseed (high oil content commodities) which show that quizalofop-p-ethyl, the free acid, and phenols 1, 2, and 4 metabolites are stable in frozen storage for at least 5 ½ months (F.Griffith, 2/21/96, PP# 5F4545/FAP# 6H5737).

For mint, adequate data were presented to demonstrate that quizalofop-p-ethyl and quizalofop acid were stable in mint hay and mint oil after up to approximately 600 days of frozen storage. These data are adequate to support the sample storage intervals in the mint magnitude of the residue and processing studies.

(f) GLN 860.1500: Crop Field Trials

Adequate residue data were provided to support a tolerance of 1.0 ppm for canola seed (see Attachments 1 and 2, F.Griffith, 2/21/96, PP# 5F4545/FAP# 6H5737).

Adequate residue data were provided to support a tolerance of 2.0 ppm for mint (see Attachment 3, S.Knizner, 5/14/96, PP#6E4652). In order to conform to the raw agricultural commodities (racs) listed in OPPTS Test Guidelines Series 860, Residue Chemistry, Table 1, (August, 1996), tolerances should be established for racs **Peppermint, tops** and **Spearmint, tops**.

(g) GLN 860.1520: Processed Food/Feed

Processing data provided indicate no concentration of residues in mint oil. No tolerances are required for mint oil (S.Knizner, 5/14/96, PP#6E4652).

Processing data provided for canola seed indicated concentration in canola meal (see Attachment 2 for details F. Griffith, 2/21/96, PP#5F4545). Based on the concentration factor of 2.3X and the highest average field trial (HAFT) residue level of 0.65 ppm for canola, **HED recommended that a 1.5 ppm tolerance be established for canola meal** (F. Griffith, 2/21/96, PP#5F4545).

(h) GLN 860.1480: Meat, Milk, Poultry, and Eggs

There are no livestock feedstuffs associated with mint (OPPTS Test Guidelines, 8/96, Table 1).

A ruminant feeding study has been submitted and reviewed in PP #s 5F3252 and 1F3951. Based on the results of this study, HED has previously concluded (F.Griffith, 2/21,96, PP#5F4545) that the established quizalofop and quizalofop-p-ethyl tolerance in milk, and in fat, meat, and meat by-products of cattle, goats, hogs, horse, and sheep are adequate and need not be increased from the additional use on canola. Additionally, the established tolerances of quizalofop and quizalofop-p-ethyl in eggs, and in

fat, meat, and meat by-products of poultry are adequate and need not be changed from the additional use on canola.

(i) GLN 860.1400: Water, Fish, and Irrigated Crops

Not applicable.

(j) GLN 860.1460: Food Handling

Not applicable.

(k) GLN 860.1850: Confined Accumulation in Rotational Crops

HED has previously concluded that the nature of the residue in rotational crops is adequately understood and is the same as identified above for tomatoes, cottonseed, soybeans, and sugar beets (F.Griffith, 2/21/96, PP# 5F4545/FAP# 6H5737). The residues of concern are quizalofop-p-ethyl and its acid metabolite, and S-enantiomers of the ester and acid.

(l) GLN 860.1900: Field Accumulation in Rotational Crops

HED has previously concluded that available data support a 120 day plant back interval (F.Griffith, 2/21/96, PP# 5F4545/FAP# 6H5737).

(m) Codex Harmonization

There are no CODEX, Canadian, or Mexican MRLs for quizalofop-p-ethyl residues in/on mint.

Since there are no Mexican or Codex Maximum Residue Limits (MRLs)/tolerances for quizalofop-ethyl in/on canola seed, compatibility is not a problem at this time. Compatibility cannot be achieved with the Canadian negligible residue type limit at 0.1 ppm as the USA use pattern had findings of real residues above 0.1 ppm. Additionally, the Canadian MRL is in terms of parent only, thus the tolerance expressions are not compatible.

(n) Dietary Exposure Assessment/Anticipated Residues

(1) Acute Dietary (Food) Risk

An acute dietary risk assessment is not required because no acute toxicological endpoints were identified for quizalofop-p-ethyl.

(2) Chronic Dietary (Food) Risk

In conducting this chronic dietary risk assessment, HED has made very conservative assumptions -- 100% of mint and canola seed and all other commodities having quizalofop-p-ethyl tolerances will contain quizalofop-p-ethyl regulable residues and those residues will be at the level of the tolerance -- which result in an

overestimation of human dietary exposure. Thus, in making a safety determination for these tolerances, HED is taking into account this conservative exposure assessment. The HED DRES System was used for the chronic dietary exposure analysis. The analysis evaluates individual food consumption as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS) and accumulates exposure to the chemical for each commodity.

Canola seed per se is not a human food item. All canola seed is processed into canola oil which is consumed. Because canola oil is not listed as a commodity in DRES, HED has developed the following standard procedure for estimating potential exposure to pesticides through consumption of canola oil. BEAD supplied data are used to help estimate a consumption value for canola as follows:

CONSUMPTION (g/kg/day) x RESIDUE (mg/kg) = EXPOSURE (mg/kg/day)

The consumption value for canola oil was taken as the U.S. production volume(877 million lbs or 3.98×10^{11} g) divided by the U.S. population in the 1977-78 USDA Food Consumption Survey (240 million) to get grams of canola oil consumed per year. Further division was done to estimate consumption per day for an average person body weight (58.9 kg) to get consumption per person per day. The expected residue value (1 ppm) was used as the residue for canola oil and 100 percent crop treated was assumed. The estimated exposure for quizalofop-p-ethyl resulting from the proposed tolerance for canola seed is 7.7×10^{-5} mg/kg bwt/day. This exposure represents 0.9% of the RfD.

$$\text{Consumption} = (3.98 \times 10^{11} \text{ g canola oil})/(2.4 \times 10^{8} \text{ persons})$$
$$= 1.66 \times 10^{3} \text{ g canola oil/person}$$

$$\frac{1.66 \times 10^{3} \text{ g/person}}{58.9 \text{ kg bwt} \times 365 \text{ day/year}} = 7.7 \times 10^{-2} \text{ g canola oil/kg bwt/day}$$
$$\text{or } 7.7 \times 10^{-5} \text{ kg canola oil/kg bwt/day}$$

With this consumption estimate, exposure can be estimated as follows:

CONSUMPTION (g/kg/day) x RESIDUE (mg/kg) = EXPOSURE (mg/kg/day)

7.7×10^{-5} kg canola oil/kg bwt/day x 1 mg quizalofop/kg canola oil = 7.7×10^{-5} mg quizalofop/kg bwt/day

This exposure represents 0.9% of the RfD.

$(7.7 \times 10^{-5}$ mg/kg bwt/day)/(0.009 mg/kg bwt/day) x 100 = 0.9%

This approach results in a conservative exposure assessment. HED notes that consumption of corn oil by the general US population in the 1977-78 USDA Food Consumption Survey was only 0.022 g/kg/day. The consumption estimate for canola oil is approximately 3.5 times this value.

The existing quizalofop-p-ethyl tolerances (published and those proposed in these petitions) result in a Theoretical Maximum

Residue Contribution (TMRC) that is equivalent to the following percentages of the RfD (note that the contribution for canola has been added to the TMRC for all other foods shown in the chronic DRES analysis presented in Attachment 4) :

Population Subgroup	TMRC (mg/kg/day)	%RfD
U.S. Population	0.000540	6.0%
Nursing Infants (<1 year old)	**0.000577**	**6.4%**
Non-Nursing Infants (<1 year old)	**0.001744**	**19%**
Children (1-6 years old)	**0.001089**	**12%**
Children (7-12 years old)	**0.000782**	**8.7%**
Females 13+ years old	0.000465	5.2
Hispanics	0.000647	7.2%
Non-Hispanic Blacks	0.000594	6.6%
Non-Hispanic Others	0.000577	6.4%
Southern Region	0.000573	6.4%

The subgroups listed above are: (1) the U.S. population (48 states); (2) those for infants, children, and females 13+ years old; and, (3) the other subgroups for which the percentage of the RfD occupied is greater than that occupied by the subgroup U.S. population (48 states).

(3) Carcinogenic Risk

Based on the cancer classification by the Cancer Peer Review Committee and the SAP, a carcinogenic risk assessment is not required.

4) Exposure from Drinking Water Sources

Estimated environmental concentrations (EECs) for quizalofop-p-ethyl have been requested from EFED but have not been provided to HED at this time.

5) Risk From Drinking Water Sources

Because no acute dietary endpoint was determined, an acute water exposure risk assessment is not required.

Based on the chronic dietary (food)exposure and using default body weights and water consumption figures, chronic drinking water levels of concern (DWLOC) for drinking water were calculated. To calculate the DWLOC, the chronic dietary food exposure was subtracted from the RfD.

Chronic RfD = 0.009 mg/kg/day
Chronic Dietary Food Exposure (DRES):
- -U.S. Population = 0.000540 mg/kg/day
- -Females (13 + years old, not pregnant, or nursing) = 0.000465 mg/kg/day
- -Non-nursing Infants <1 year old = 0.001744 mg/kg/day

US Population
RfD 0.009000
Food Exposure -.000540
Max H_2O Exposure 0.008460 mg/kg/day

Females (13 + years old, not pregnant or nursing)
RfD 0.009000
Food Exposure -.000465
Max H_20 Exposure 0.008535 mg/kg/day

Non-nursing Infants
RfD 0.009000
Food Exposure -.001744
Max H_20 Exposure 0.007256 mg/kg/day

The following formulas were used to convert maximum allowable water exposure to ppb. The 2 liters (L) of drinking water consumed/day by adults and the 1 L per day consumed by children are default assumptions. The Agency's **default** body weights for males is 70 kg and for females, 60 kg. HED's default body weight for children is 10 kg.

US Population DWLOC = **296 ppb**
(chemical concentration in μg/L in consumed water) * (10^{-3} mg/μg) ÷ (70 kg body weight) * (2 L water consumed/day)

0.008460 mg/kg/day = X ug/L * 10^{-3} mg/ug * 2L)/ 70kg
296 ug/L = X

Female (13+ years old, not pregnant or nursing) DWLOC = **256 ppb**
(chemical concentration in μg/L in consumed water) * (10^{-3} mg/μg) ÷ (60 kg body weight) * (2 L water consumed/day)

0.008535 mg/kg/day = (X ug/L * 10^{-3} mg/ug * 2L) / 60 kg
256 ug/L = X

Infant/Children DWLOC = **73 ppb**
(chemical concentration in μg/L in consumed water) * (10^{-3} mg/μg) ÷ (10 kg body weight) * 1 L water consumed/day)

0.007256 mg/kg/day = (X ug/L * 10^{-3} mg/ug * 1L) / 10 kg
73 ug/L = X

For chronic exposure, based on an adult body weight of 70 kg and 2L consumption of water per day, RAB2's level of concern from chronic exposure estimates for the US Population is 296 ppb and 256 ppb for females 13 years and older, not pregnant or nursing. For non-nursing infants (10 kg and 1L water/day) our level of concern for drinking water is 73 ppb.

6) Combined Dietary Risk from Food and Water Sources

Provided EFED estimates of quizalofop-p-ethyl chronic residues in drinking water are less than 73 ppb, aggregate (food, water, and

residential) chronic exposure for infants, children, and adults will not exceed HED's level of concern.

e. Food Quality Protection Act Considerations

1) Cumulative Risk

Quizalofop-p-ethyl is a member of the oxyphenoxy acid ester class of pesticides (Ware, *Fundamentals of Pesticides, 3rd Ed.*). Other members of this class include fluazifop-butyl, diclofop-methyl, fenoxaprop-ethyl, and haloxyfop-methyl.

Section 408(b)(2)(D)(v) of the Food Quality Protection Act requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will increase the Agency's scientific understanding of this question such that EPA will be able to develop and apply scientific principles for better determining which chemicals have a common mechanism of toxicity and evaluating the cumulative effects of such chemicals. The Agency anticipates, however, that even as its understanding of the science of common mechanisms increases, decisions on specific classes of chemicals will be heavily dependent on chemical-specific data, much of which may not be presently available.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

HED does not have, at this time, available data to determine whether quizalofop-ethyl has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this tolerance action, therefore, HED has not assumed that quizalofop-ethyl has a common mechanism of toxicity with other substances.

2) Endocrine Disruption

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disrupter effects.

3) Aggregate Exposure and Risk Assessment/Characterization

(a) Acute, short-term, and intermediate-term aggregate risk

An acute aggregate risk assessment is not required because no acute, short-term, and/or intermediate-term toxicological endpoints were identified for quizalofop ethyl.

(b) Chronic aggregate risk

Because there are no indoor or outdoor residential uses for quizalofop-p-ethyl, provided EFED estimates of quizalofop-p-ethyl chronic residues in drinking water are less than 73 ppb, aggregate (food, water, and residential) chronic exposure for infants, children, and adults will not exceed HED’s level of concern.

CC with attachments: PP#6E4652, PP#5F4545, Reading File, S. Knizner

MEMORANDUM

Subject: **PP# 5F4545/FAP# 6H5737 - QUIZALOFOP-P ETHYL ESTER (ASSURE® II) ON THE FOLIAGE OF LEGUME VEGETABLES (EXCEPT SOYBEANS) CROP GROUP, CANOLA AND CANOLA PROCESSED COMMODITIES.**
Review of Magnitude of the Residue Data and Residue Analytical Method.
(MRID #s 436957-01 and 436957-02)[CBTS #s 16392, 16393, and 16394]{DP Barcode D220476, D220478, and D220478}

From: Francis D. Griffith, Jr., Chemist
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Health Effects Division (7509C)

To: Robert J. Taylor, PM-25
Herbicide-Fungicide Branch
Registration Division (7505C)

and

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Risk Characterization and Analysis Branch
Health Effects Division (7509C)

Thru: E. Zager, Acting Chief
Chemistry Branch I - Tolerance Support
Health Effects Division (7509C)

INTRODUCTION

E.I. duPont de Nemours and Company, Agricultural Products, proposes tolerances for the combined residues of the herbicide quizalofop-p ethyl ester, trade named Assure® II (ethyl(R)-2-[4-((6-chloroquinoxalin-2-yl)oxy)phenoxy] propionate), and the racemic quizalofop ethyl ester, trade named Assure® (ethyl-2-[4-((6-chloro-quinoxalin-2-yl)oxy)phenoxy] propionate) and the acid metabolite (ethyl 2-[4-((6-chloroquinoxalin-2-yl)oxy)phenoxy] propanoic acid), all expressed as quizalofop ethyl ester in or on the following raw agricultural commodities (racs): the forage of legume vegetables (except soybean) crop group at 3 ppm and canola at 2 ppm. A feed additive tolerance (FAT) is proposed for canola meal at 3 ppm and a food additive tolerance is proposed for canola oil at 0.1 ppm.

EXECUTIVE SUMMARY OF RESIDUE CHEMISTRY DEFICIENCIES

- CONDITIONALLY COMPLETE THE TMV
- ADDITIONAL FIELD TRIAL RESIDUE DATA FOR FOLIAGE OF LEGUME VEGETABLES

RECOMMENDATION

CBTS cannot recommend at this time for the requested permanent tolerances for the combined residues of the herbicide quizalofop ethyl ester and the acid, all expressed as quizalofop ethyl ester in or on canola seed 2 ppm, the forage of legume vegetables (except soybean) crop group at 3 ppm, and FAT for canola meal at 3 ppm and canola oil at 0.1 ppm for the reasons cited above in our Executive Summary and further described in the conclusions 6b; 8b, e, and f; and 9.

Provided a revised Section F is submitted to address conclusions 8b and f, and 9; CBTS could recommend for tolerances with expiration dates for total quizalofop ethyl to allow DuPont time to plan and conduct additional foliage of legume vegetable field trials, analyze the samples, and present a final report to the Agency. While the granting of registrations and the issuing of tolerances is the prerogative of the Registration Division, CBTS suggests that total quizalofop ethyl tolerances be set as we suggested in our conclusions above.

A DRES analysis may now be initiated using the CBTS suggested revised total quizalofop ethyl ester tolerances on canola seed at 1 ppm and canola meal at 1.5 ppm. There is no anticipated concentration of quizalofop ethyl in canola oil. A DRES analysis may be initiated for the foliage of the legume vegetables (except soybeans) crop group at 3 ppm.

CONCLUSIONS

Note: All residue chemistry data for the foliage of legume vegetables (except soybeans) crop group were submitted in PP# 3F4268 and reviewed by F. Griffith in the March 30, 1995, memorandum (qv).

1. CBTS Conclusion on **Product Chemistry/Chemical Identity**

CBTS concludes that after reviewing the CSF for the TGAI the impurities present in the TGAI quizalofop-p ethyl ester are not expected to present a residue problem in the subject crops when formulated into Assure® II and used as directed.

2. CBTS Conclusion on **Directions for Use/Labeling**

The petitioner has proposed an adequate set of directions for use of quizalofop-p methyl ester, formulated as Assure® II, in conjunction with an approved oil concentrate, or a non-ionic surfactant on canola and crambie.

3. CBTS Conclusion on the **Nature of the Residue - Plants**

CBTS reiterates that the nature of the quizalofop-p ethyl ester residue in **cottonseed**, potatoes, soybeans, tomatoes and sugarbeets is adequately understood. The residues of concern are quizalofop-p ethyl ester and its acid metabolite, quizalofop-p,

and the S enantiomers of both the ester and the acid, all expressed as quizalofop-p ethyl ester. We are translating these data to canola.

4. CBTS Conclusion on the **Nature of the Residue - Livestock**

The nature of the quizalofop ethyl ester residue in livestock is adequately understood. The residues of concern are quizalofop ethyl, quizalofop methyl, and quizalofop, all expressed as quizalofop ethyl.

5. CBTS Conclusion on **Confined Accumulation Studies on Rotational Crops**

The petitioner has characterized and identified over 50% of the residue in each of the rotational crops from the labeled quizalofop ethyl soil treatment and has confirmed the metabolic pathways. The nature of the residue in rotational crops is adequately understood and is the same as identified above for tomatoes, cottonseed, soybeans, and sugar beets. The residues of concern are quizalofop ethyl and its acid metabolite.

6. CBTS Conclusions on the **Residue Analytical Method**

a. The petitioner has presented adequately validated residue analytical methods, LAN-1 and LAN-3, to gather the magnitude of the quizalofop-p, its acid metabolite; and phenols 1, 2, and 4 residue data on canola and canola processed commodities.

b. The revised residue analytical method for quizalofop-p and its acid metabolite as presented in PP# 3F4268 has been submitted for a Tolerance Method Validation (TMV) in EPA laboratories. The Analytical Chemistry Branch (ACB) noted several deficiencies in the method. The petitioner needs to respond to ACB's concerns with a revised method before we can get the TMV back on track. CBTS reiterates that the results of the successful TMV is not a prerequisite for a tolerance on canola and canola processing commodities as there is already an enforcement method in PAM-II.

7. CBTS Conclusion on **Storage Stability**

The petitioner has provided frozen storage stability data for quizalofop acid, phenols 2, 3, and 4 in cottonseeds and cotton processed commodities, snap bean pods and "straw," peas and pea forage, sugarbeet roots, and **canola** which show residues are stable for up to 3 years. The data are sufficient to support the magnitude of the residue crop field trial data submitted in this petition where samples were stored under like conditions and for a shorter time.

8. CBTS Conclusions on **Magnitude of the Residue - Crop Field Trials**

a. The petitioner has generated more than the required total number of quizalofop on canola trials as specified in our June 1994 guidance. Although fewer trials were conducted in Region XI than suggested in that guidance document the petitioner generated all of the canola field trial data in 1989, prior to the new requirements. We can recommend for a quizalofop ethyl ester tolerance on canola without any additional crop field trial residue data.

b. CBTS concludes that quizalofop and its metabolites, all expressed as quizalofop-p ethyl ester, are not expected to exceed the proposed 2 ppm tolerance on canola when Assure® II plus the surfactant are used as directed. However, this tolerance is higher than necessary (see conclusion 8f below).

c. CBTS reiterates that there has been insufficient time since the imposition of the data requirement for specific geographical representation on bean field trials to generate the necessary residue data. We continue to recommend for tolerances with an expiration date for total quizalofop residues on the foliage of legume vegetables crop group to allow the company time to complete the trials, analyze the samples, and present a final report (see PP# 3F4268 memo by F. Griffith dated 14 Feb 96). While the granting of a registration and a tolerance is the prerogative of the Registration Division, CBTS suggests quizalofop-p tolerances with a 3 year expiration date are acceptable considering we are too far into the 1996 growing season for the company to adequately plan for these additional field trials. This should allow sufficient time to complete the trials even with crop failure, analyze the samples, and present a final report.

d. The petitioner needs to present the following additional quizalofop-p ethyl ester magnitude of the residue crop field trial data for succulent beans and forage: 1 trial from Region I, 1 trial from Region II, and 1 trial from Region III.

e. CBTS reiterates that the petitioner has presented an adequate amount of varietal and geographically representative pea and bean crop field trial residue data to show that residues of quizalofop and quizalofop-p ethyl ester are not expected to exceed the proposed foliage of legume vegetables (except soybeans) crop group tolerance of 3 ppm when Assure® II plus the surfactant are used as directed. This conclusion is drawn for a time limited tolerance only.

f. Since CBTS recommends for tolerances no higher then necessary, the petitioner will need to submit a revised section F proposing total quizalofop ethyl tolerances for canola at 1 ppm for 40 CFR §180.441(a) and for the foliage of legume vegetables subgroup foliage of legume vegetables (except soybeans) at 0.5 ppm for 40 CFR §180.441 (c).

9. CBTS Conclusion on **Magnitude of the Residue - Processed Food/ Feed**

The petitioner has conducted an adequate canola processing study using canola bearing detectable residues following a single 6X exaggerated application with a 45 day PHI. Total quizalofop residues were shown to concentrate only in canola meal. Residues declined in canola oil. In a revised Section F the petitioner will need to propose a total quizalofop Section 701 Maximum Residue Limit (MRL) on canola meal at 1.5 ppm. The petitioner needs to delete the proposed total quizalofop ethyl tolerances for canola oil in the revised section F.

10. CBTS Conclusions on **Magnitude of the Residue - Meat/Milk/ Poultry/Eggs**

a. The results of the quizalofop ethyl ester bovine feeding study show that finite residues will actually occur in milk and livestock tissues from the feeding of quizalofop ethyl ester treated racs or their processed feed items when Assure® II is used as directed. The established quizalofop and quizalofop ethyl ester tolerances in milk, and in fat, meat, and meat by-products of cattle, goats, hogs, horses, and sheep are adequate and need not be increased from these additional uses.

b. The results of the quizalofop ethyl ester poultry feeding study show that while it is not possible to establish with certainty whether finite residues will actually occur in eggs and tissues from the feeding of quizalofop ethyl ester treated racs or their processed feed items when Assure® II is used as directed, there is a reasonable expectation for such residues to occur. The established quizalofop and quizalofop ethyl ester tolerances in eggs, and in fat, meat, and meat by-products of poultry are adequate and need not be changed from these additional uses.

11. CBTS Conclusion on **Harmonization of Tolerances**

Since there are no Mexican or Codex MRLs/tolerances, compatibility is not a problem at this time. Compatibility cannot be achieved with the Canadian negligible residue type limit at 0.1 ppm as the USA use pattern had findings of real residues above 0.1 ppm.

DETAILED CONSIDERATIONS

BACKGROUND

Tolerances of the combined residues of the racemic mixture of quizalofop ethyl and its acid metabolite quizalofop, all expressed as quizalofop ethyl have been established on soybeans at 0.05 ppm (see 40 CFR §180.441[a]). A food additive tolerance (FAT) has been established for the combined residues of the racemic mixture of quizalofop ethyl on soybean flour at 0.5 ppm (see 40 CFR §185.5250) and feed additive tolerances have been

established for combined residues of the racemic mixture on soybean hulls at 0.2 ppm, on soybean meal at 0.5 ppm, and on soybean soapstock at 1 ppm (see 40 CFR §186.5250). CBTS has also recommended for the established tolerance of combined residues of the R enantiomer quizalofop-p ethyl ester and its acid metabolite, quizalofop-p, and the S enantiomers of both the ester and the acid, all expressed as quizalofop-p ethyl ester on cottonseed and pineapples at 0.1 ppm (see 40 CFR §180. 441[c]).

In addition, CBTS has recommended for two Emergency Exemptions (Section 18) for use of quizalofop-p ethyl ester on mint (see memoranda by M. Peters dated February 25, 1993, for 93WA0008 and 93MT0004). Quizalofop-p ethyl ester and its metabolite residues are not expected to exceed 5 ppm on mint hay and 0.05 ppm in mint oil.

In a related co-pending petition residue chemistry data have been presented for the foliage of legume vegetables to support a crop group tolerance at 0.7 ppm. PP# 3F4268 is currently in reject status with deficiencies on the method needing to complete a successful Agency TMV, a revised tolerance, and additional crop field trial residue data (see memo dated March 30, 1995 and February 14, 1996).

PRODUCT CHEMISTRY/CHEMICAL IDENTITY

The product chemistry data for the R enantiomer were submitted as an amended registration to PP# 3F3252/6H5479.

CBTS concludes that after reviewing the results of the preliminary analysis of the TGAI (contains 98% active ingredient) as presented on the Confidential Statement of Formula (CSF) the impurities present in the TGAI quizalofop-p ethyl ester are not expected to present a residue problem in canola and crambie when formulated into Assure® II and used as directed.

DIRECTIONS FOR USE/LABELING

Quizalofop-p ethyl ester is proposed for use as a selective post emergence herbicide to provide control of annual grasses; eg, fox-tails, barnyardgrass, etc., and perennial grasses; eg, quackgrass.

The formulation to be used on the crops is Assure® II Herbicide (EPA Reg. No. 352-541) containing quizalofop-p ethyl ester at 10.3%, or 0.88 lb a.i. per gallon. In ground applications, apply with standard fan or hollow cone nozzles, not with flood type nozzles. Apply in a minimum of 10 to 20 gallons water per acre, and use either an EPA approved crop oil concentrate at a rate of 4 qts per 100 gallons (1%), or a non-ionic surfactant at a rate of 1 qt per 100 gallon (0.25%). For aerial application, apply in a minimum of 5 gallons water per acre.

To control annual and perennial grasses in canola and crambie apply 7 to 12 ozs of Assure® II (1.2 ozs ai quizalofop-p

ethyl ester per 3/4 pt) per acre per application once or twice per crop growing season when the grasses are actively growing, usually when they are around 4 inches high. The maximum application in a crop growing season to canola is 18 ozs Assure® II (2 ozs ai) with a 60 day PHI.

The petitioner cautions that the cereal grains are "highly sensitive" to Assure II, thus care should be taken to avoid application when drift is likely. Assure II should not be applied through any irrigation system.

The petitioner has proposed an adequate set of directions for use of quizalofop-p methyl ester, formulated as Assure® II, in conjunction with an approved oil concentrate or a non-ionic surfactant on canola and crambie.

NATURE OF THE RESIDUE - PLANTS

The registrant has provided plant metabolism studies for soybeans, cotton, tomatoes, potatoes, and sugarbeets. These studies have been previously reviewed in PP# 3F4268.

In summary, quizalofop-p ethyl ester is metabolized by cleavage at three sites as follows:

1) Primary pathway is hydrolysis of the ethyl ester to form the quizalofop-p acid, then

2) Cleavage of the enol ether linkage in the acid, between the phenyl and quinoxalinyl rings, to form phenols, and

3) Cleavage of the ether linkage between the isopropanic group and the phenyl ring to form a phenol.

The plant metabolism data show that quizalofop-p ethyl ester does not translocate, but is rapidly hydrolyzed to the corresponding acid, then the phenols conjugate with the plant sugars. Metabolism studies in soybeans using the racemic mixture quizalofop ethyl ester and the resolved D+ isomer show nearly identical pathways.

CBTS reiterates that the nature of the quizalofop-p ethyl ester residue in cottonseed, potatoes, tomatoes, soybeans, and sugarbeets is adequately understood. The residues of concern are quizalofop-p ethyl ester and its acid metabolite, quizalofop-p, and the S enantiomers of both the ester and the acid, all expressed as quizalofop-p ethyl ester. CBTS is translating these data to canola.

NATURE OF THE RESIDUE - LIVESTOCK

^{14}C-phenyl and ^{14}C-quinoxaline quizalofop ethyl ester caprine and poultry metabolism studies have been submitted and reviewed.

In summary, the primary pathway in ruminants is hydrolysis of the ethyl ester to form the quizalofop-p acid, then methyl esterification to form the quizalofop methyl ester. Since neither phenol 1 or phenol 2 were detected, cleavage of the enol

ether linkage in the acid between the phenyl and quinoxalinyl rings and cleavage of the ether linkage between the isopropanic group and the phenyl ring are not ruminant metabolic pathways.

In poultry, the primary metabolic pathway is also the hydrolysis of the ethyl ester to form the quizalofop-p acid, then the methyl esterification to form the quizalofop methyl ester becomes a minor pathway. Poultry apparently recognize the free acid metabolite as a fatty acid and utilize it in fatty acid chain elongation to form the quizalofop-pentanoic acid metabolite through a series of reactions involving acetyl Co-A, NAD/NADPH, and catalyzed by beta-hydroxyaryl dehydrogenase and enoyl reductase. Since neither phenol 1 or phenol 2 were detected, cleavage of the enol ether linkage in the acid between the phenyl and quinoxalinyl rings and cleavage of the ether linkage between the isopropanic group and the phenyl ring are not poultry metabolic pathways.

The nature of the quizalofop ethyl ester residue in livestock is adequately understood. The residues of concern are quizalofop ethyl, quizalofop methyl, and quizalofop, all expressed as quizalofop ethyl.

CONFINED ACCUMULATION STUDIES ON ROTATIONAL CROPS

In summary, [Phenyl-^{14}C] and [quinoxaline-^{14}C] quizalofop ethyl treated soils were aged 30 and 62 days before planting with the rotational crops red beets, lettuce, wheat, peanuts, and cotton. The petitioner has characterized and identified over 50% of the residue in each of the rotational crops from the phenyl and quinoxaline labeled quizalofop ethyl soil treatment and has confirmed the hydrolysis of the ethyl ester, and the cleavage of the enol and ether linkages metabolic pathways. These data support a 120 day plant back interval.

The nature of the residue in rotational crops is adequately understood and is the same as identified above for tomatoes, cottonseed, soybeans, and sugar beets. The residues of concern are quizalofop ethyl and its acid metabolite.

RESIDUE ANALYTICAL METHOD

The petitioner presented the magnitude of the residue data which were generated by Enviro-Test Laboratories, 9936-67 Avenue, Edmonton, Alberta T6E OP5. The method used for quizalofop ethyl ester and its acid metabolite was referred to as LAN-1. The method was previously reviewed by F. Griffith in his March 30, 1995, memorandum in PP# 3F4268 (qv).

In summary, samples were extracted twice with ACN/1% HOAc, centrifuged and combined. The ACN was removed by rotary evaporation and the aqueous extract was adjusted to pH 5 before cellulase and beta-glucosidase were added. The sample was incubated for 2 hours, then the pH was adjusted to 8 and the sample was hydrolyzed an additional 2 hours after addition of esterase. The sample was cooled, pH adjusted to 3, then partitioned twice with ACN/CH_2Cl_2. The extracts were combined, concentrated by rotary evaporation, transferred into ACN, then

partitioned twice with hexane (discard the hexane). KH_2PO_4 buffer was added; the sample was mixed, centrifuged, and filtered. The sample was cleaned up on a prep or cleanup HPLC column reliance cartridge with a "heart cut" collected which contained quizalofop and reanalyzed by HPLC using a Supelco C_{18} column with the mobile phase of 22% ACN/K_2HPO_4 at 1.5 ml/min flow rate and detection by UV at 254 nm. Quantitation was by peak height. Acceptable linearity curves were presented.

The limit of quantitation (LOQ) is 0.05 ppm with a set of 12 samples being analyzed in 3 working days.

To validate the method control samples of canola seeds were fortified with quizalofop at 0.047/0.049, 0.19/0.2, and 0.47/0.49 ppm. Overall quizalofop recoveries ranged from 71 to 113%, averaging 86 $\pm$ 15%, n = 6.

Concurrent quizalofop and quizalofop-p recoveries from control canola seeds spiked at 0.047 to 0.47 ppm ranged from 70 to 95%, averaging 82 $\pm$ 9%, n = 7. These fortified samples were analyzed along with the treated canola samples.

Method and concurrent validation data for quizalofop and its acid metabolite from the foliage of legume vegetables were previously submitted and reviewed (ibid).

The petitioner presented additional magnitude of the residue data which were also generated by Enviro-Test Laboratories. The method used for quizalofop ethyl ester phenol 2 and phenol 4 metabolites was referred to as LAN-3. The method was previously reviewed by F. Griffith in his March 30, 1995, memorandum in PP#3F4268 (qv).

In summary, samples were extracted twice with aqueous ACN, centrifuged, filtered, acidified with 10% HCl, and partitioned with CH_2Cl_2 to remove the unconjugated phenols. The aqueous layer was adjusted to pH 5, then incubated with beta-glucosidase and cellulase. After incubation, the aqueous layer was adjusted to pH 2 and partitioned again with CH_2Cl_2. The CH_2Cl_2 extracts were combined and rotary evaporated to just dryness. ACN was used to dissolve the sample before it was partitioned three times with hexane (discard hexane). The sample was blown dry at room temperature under a gentle stream of N_2. The sample was derivatized with diazomethane, then cleaned-up through a deactivated florisil column. The methyl esters of phenol 2 and phenol 4 were eluted off the column with acetone/ hexane. Determination was by capillary GC-MSD using a HP 5890 GC containing a J & W DB 1701, 25 m X 0.25 mm column connected to a HP 5971 MSD. Ions 165 or 124 were used for identification and quantitation of phenol 2 and ions 210 or 123 were used for identification and quantification of phenol 4.

The LOQ is 0.05 ppm for both phenols and a set of 12 samples can be analyzed within 2 days.

Control samples of canola seeds were fortified with quizalofop phenol 2 and 4 at levels around 0.046, 0.23, and 0.46 ppm. Overall quizalofop phenol 2 recoveries ranged from 100 to

124%, averaging 114 ± 9% and quizalofop phenol 4 recoveries ranged from 75 to 83% averaging 79 ± 4%, n = 6.

Concurrent quizalofop phenol 2 and phenol 4 recoveries from canola seeds spiked at 0.046 to 0.46 ppm ranged from 67 to 122%.

The petitioner has generated adequate method validation and concurrent method validation data to show that methods LAN-1 and LAN-3 are suitable to gather the magnitude of the quizalofop-p ethyl ester and its metabolites residue crop field trial data.

The revised residue analytical method for quizalofop-p and its acid metabolite as presented in PP# 3F4268; ie, LAN-1, has been submitted for a Tolerance Method Validation (TMV) in EPA laboratories. The Analytical Chemistry Branch (ACB) noted several deficiencies in the method (see memoranda by H. Hundley dated 21 July 95). The petitioner needs to respond to ACB's concerns with a revised method before we can get the TMV back on track. CBTS reiterates that the results of the successful TMV is not a prerequisite for a tolerance on canola and canola processing commodities.

STORAGE STABILITY

Storage stability data have been previously submitted for soybeans and cottonseed (high oil content commodities) which show that quizalofop ethyl ester, the free acid, and phenols 1, 2, and 4 metabolites are stable in frozen storage for at least 5 1/2 months.

The petitioner submitted additional frozen storage stability data for quizalofop ethyl ester, its acid and phenol metabolites in cottonseed, beans, peas, sugarbeets, and canola which have been reviewed by F. Griffith in his memoranda dated March 30, 1995, and February, 1996 (qv).

These frozen storage stability data for quizalofop acid, phenols 2, 3, and 4 in cottonseeds and cotton processed commodities, snap bean pods and "straw," peas and pea forage, sugarbeet roots, and **canola** show that residues are stable for up to 3 years. The data are sufficient to support the magnitude of the residue crop field trial data submitted in this petition where samples were stored under like conditions and for a shorter time.

MAGNITUDE OF THE RESIDUE - CROP FIELD TRIALS

CANOLA (MRID # 436957-01)

The petitioner presented quizalofop residue data on canola in a study titled "Magnitude of Residues of Assure® II Herbicide When Applied to Canola" by T. Mester dated June 9, 1993, and coded Dupont Report Number AMR 1389-89.

The petitioner presented total quizalofop-p magnitude of the residue data on canola seeds from 9 crop field trials in 5 states: Washington, North Dakota, Minnesota, Illinois, and

Tennessee all for the 1989 crop year on 3 varieties. When the number of crop field trials presented are reviewed against the data requirements for number of trials as described in the "EPA Guidance on Number and Location of Domestic Crop Field Trials for Establishment of Pesticide Residue Tolerances", June 1994, the petitioner appears to need 2 additional canola field trials from Region XI. CBTS notes that the petitioner has generated more than the required total number of canola field trials specified in the June 1994 document. Although fewer trials were conducted in Region XI than suggested in that guidance document the petitioner generated all of the field trial data prior to the new requirements. We can recommend for a quizalofop ethyl ester tolerance on canola without any additional crop field trial residue data.

Each trial had a control plot and 2 test plots. One canola test plot received 1 broadcast ground spray at 1.5 oz ai (approx. 1X)/acre along with the surfactant. The application was post-emergence, when the canola was flowering, or at least 4 inches high. The other canola plot received 1 broadcast ground spray at a rate of 3 oz ai (2X)/acre with the surfactant. Both the 1X and 2X applications were done at the same time. One of the Minnesota trials did not produce seed after the Assure® II application due to a lack of rain and an early frost. The test sites in Tennessee received the racemic Assure® application and the test site in the other four states received Assure® II containing the D+ isomer. Neither of these situations affect the validity of the data presented.

2.5 pounds of mature canola seeds were harvested at 38 to 74 days PHI. Samples were promptly frozen and remained frozen until preparation and analysis. Samples were analyzed by the residue analytical methods reviewed above which have adequate validation and concurrent recovery data for quizalofop ethyl ester and the phenol metabolites.

Residues of quizalofop and phenols 2 and 4 were not detected to the LOQ of 0.05 ppm in any of the control canola seeds.

From the 1X application, detectable quizalofop residues ranged from < 0.05 ppm (3 trials) to 0.7 ppm, averaging 0.22 $\pm$ 0.22 ppm, n = 12. **The highest average field trial (HAFT) for the 1X application is 0.65 ppm.** From the 2X application, quizalofop residues ranged < 0.05 ppm (2 trials) to 1.5 ppm, averaging 0.45 $\pm$ 0.44 ppm.

No phenol 2 or phenol 4 residues were detected in any of the canola seed samples from the 1X and 2X applications at any of PHIs.

CBTS concludes that quizalofop and its metabolites, all expressed as quizalofop-p ethyl ester, are not expected to exceed the proposed 2 ppm tolerance on canola seed when Assure® II is used as directed. However, since CBTS recommends for tolerances no higher than necessary, the petitioner will need to submit a revised Section F proposing a 1 ppm total quizalofop ethyl tolerance on canola seed in 40 CFR §180.441(a).

SUCCULENT AND DRIED PEAS

In PP# 3F4268, the petitioner presented quizalofop residue data on edible and dried peas and pea forage and "straw." These data have been reviewed by F. Griffith in his March 30, 1995, memorandum (qv).

CBTS reiterates that the petitioner has presented an adequate number of geographically representative quizalofop-p pea crop field trials.

Residues of quizalofop and phenols 2 and 4 were not detected to the LD of 0.02 ppm in any of the control succulent peas, forage, dried peas, and "straw."

Quizalofop residues were detected from the 1X application at 30 days PHI in pea forage, ranging from 0.061 to 0.28 ppm averaging 0.112 $\pm$ 0.071 ppm and from the 2X application ranging from 0.067 to 0.47 ppm averaging 0.16 $\pm$ 0.12 ppm. No phenol 2 or phenol 4 residues were detected in the succulent peas, forage, dried peas, and "straw" samples from the 1X and 2X applications at either 30 day or 60 day PHI.

On pea "straw," quizalofop residues ranged from 0.053 ppm to 0.22 ppm and averaged 0.082 $\pm$ 0.044 ppm from the proposed use application and from 0.059 to 0.32 ppm and averaged 0.126 $\pm$ 0.078 ppm from the 2X application.

The petitioner has presented an adequate amount of varietal and geographically representative pea crop field trial residue data to show that residues of quizalofop and quizalofop-p ethyl ester are not expected to exceed the proposed foliage of legume vegetables (except soybeans) crop group tolerance of 3 ppm when Assure® II plus the surfactant are used as directed. This conclusion is drawn for a time limited tolerance.

SUCCULENT AND DRIED BEANS

The petitioner presented quizalofop residue data on succulent (snap) and dried beans and bean forage and "straw" in PP#3F4268 which have been reviewed by F. Griffith in his March 30, 1995, memorandum.

CBTS reiterates that the petitioner needs to present the following additional quizalofop-p ethyl ester magnitude of the residue crop field trial data for succulent beans and forage: 1 trial from Region I, 1 trial from Region II, and 1 trial from Region III.

Residues of quizalofop and phenols 2 and 4 were not detected to the LD of 0.02 ppm in any of the control succulent beans, forage, dried beans, and "straw."

Two bean forage samples at the 30-day PHI from the 1.25X application showed detectable quizalofop residues less then the LOQ of 0.05 ppm. From the 1.25X application at 15-day PHI, 3 bean forage samples were positive for quizalofop with residues ranging from 0.02 to 0.22 ppm and averaged 0.13 $\pm$ 0.07 ppm. Quizalofop residues were detected from the two 1.25X applications

at 15 days after the second application in bean forage ranged from < 0.05 to 0.10 ppm, averaging 0.07 ± 0.02 ppm. From the 2.5X application at 15-day PHI residues in bean forage ranged from 0.02 to 0.63 ppm, averaging 0.19 ± 0.2 ppm.

No phenol 2 or phenol 4 residues at or above the LOQ of 0.05 ppm were detected in the succulent beans, bean forage, and dried beans samples from any of the four quizalofop treatments at various PHIs.

On bean "straw," quizalofop residues following the 2.5X application with a 45 day PHI ranged from 0.02 to 0.19 ppm, averaging 0.1 ± 0.05 ppm and from the 30 day PHI following the 2.5X application, residues ranged from 0.02 to 0.67 ppm averaging 0.28 ± 0.23 ppm. Applying two applications at a rate of 1.5 ozs ai/application, then harvest after 70 days, quizalofop residues ranged from 0.02 ppm to 0.11 ppm, averaging 0.06 ± 0.02 ppm. Quizalofop residues on bean "straw" following the 5X application ranged from 0.051 to 2.5 ppm, averaging 0.48 ± 0.83 ppm.

CBTS concludes that quizalofop and its metabolites, all expressed as quizalofop-p ethyl ester, are not expected to exceed the proposed foliage of legume vegetables (except soybeans) crop subgroup tolerance of 3 ppm when Assure® II plus the surfactant are used as directed. This conclusion is drawn for a time limited tolerance. However, since CBTS recommends for tolerances no higher than necessary, the petitioner will need to submit a revised Section F proposing a time limited tolerance for the foliage of legume vegetables subgroup foliage of legume vegetables (except soybeans) at 0.5 ppm for 40 CFR §180.441 (c).

MAGNITUDE OF THE RESIDUE - PROCESSED FOOD/FEED (MRID # 436957-02)

The petitioner submitted the results of a quizalofop canola processing study in a document titled "Magnitude of Residues of Assure® II Herbicide in Canola and Its Processed Fractions" by T. Mester dated June 30, 1993, and coded DuPont study number AMR 1435-89.

The canola processing study was conducted using canola grown in 1990 in Illinois, treated once at a rate of 9 ozs ai/acre (6X for an individual application) as a broadcast foliar spray with the surfactant at a rate of 0.25% (v/v) 45 days before harvest. Mature canola seeds (rac) had residues of quizalofop 0.45 ppm and phenol 2 at 1.7 ppm. The treated canola seeds were processed by the Food and Protein Research and Development Center at Texas A & M University using a small scale commercial process into light impurities, small screen-ings, large screenings, crude and **refined oil**, presscake and extracted presscake or **meal**, and soapstock. Quizalofop was detected in the extracted presscake or meal at 1.04 ppm (2.3 X conc. factor) and in the refined oil at 0.05 ppm (0.11 X conc. factor). While quizalofop residue data were presented for all of the canola processed fractions, only canola meal and oil are significant commercial processed commodities. The petitioner has conducted an adequate canola process-

ing study using canola bearing detectable residues following a single 6X exaggerated application with a 45-day PHI. Total quizalofop residues were shown to concentrate only in the canola meal. No food additive tolerance (FAT) is required for quizalofop in refined canola oil.

In determining the need for a Section 701 Maximum Residue Limit (MRL), or Section 409 feed additive tolerance (FAT) we note there was only one canola processing study and that the concentration factor for canola meal 2.3X. The HAFT from the crop field trials is 0.65 ppm. The residue level in the processed meal is obtained by multiplying the HAFT of 0.65 ppm from the 1X application X the concentration factor of 2.3 = 1.5 ppm. Canola meal is **NOT** a ready-to-eat (RTE) feedstuff. When mixed into feed concentrates and/or supplements, the dilution factor is 4. Canola meal does not exceed 15% of any total livestock diets, or 25% of concentrates or supplements . Thus, when canola meal is presented to livestock, CBTS expects the maximum residue level to be 0.375 ppm (1.5 ppm/4 = 0.375 ppm). Since the residues in the "RTE form" of canola meal do not exceed the canola seed 408 tolerance of 1 ppm, then the petitioner needs to submit a revised Section F proposing a canola meal quizalofop Section 701 MRL at 1.5 ppm.

MAGNITUDE OF THE RESIDUE - MEAT/MILK/POULTRY/EGGS

RUMINANTS

A ruminant feeding study has been submitted and reviewed in PP #s 5F3252 and 1F3951. In summary, 3 group of 3 lactating dairy cows (plus a control group) were fed 0.1, 0.5, and 5.0 ppm quizalofop ethyl ester encapsulated for 28 consecutive days. Milk was collected daily and a sub-sample was divided into skim milk and cream. 2 cows were sacrificed after 28 days with samples of fat, skeletal muscle, liver, and kidney being collected and analyzed. The remaining cow in each test group was fed a regular diet without encapsulated quizalo-fop ethyl ester for 7 additional days before sacrifice. Whole milk, skim milk, and cream from the control, and the 0.1 and 0.5 ppm dose groups showed no quizalofop to <0.02 ppm (0.05 ppm in cream). From the 5 ppm dose, quizalofop residues ranged from 0.01 to 0.02 ppm in whole milk, and when these samples were separated into cream and skim milk, the quizalofop partitioned into the cream with residues pla-
teauing at 0.26 to 0.31 ppm. No quizalofop to < 0.02 ppm was detected in skeletal muscle, and to < 0.05 ppm was detected in any liver or fat sample from any of the 3 doses. Quizalofop was detected in one kidney sample at 0.05 ppm from the 5 ppm dose.

Bovine feed items in this petition include canola meal at 15% in beef and dairy cattle diets which will contribute up to 0.23 ppm potential dietary burden. Bean forage can be in dairy cattle diets up to 60% and up to 30% in beef cattle diets for potential dietary burdens of 0.6 and 1.2 ppm respectively. Bean hay/straw can be fed to beef and dairy cattle; however the petitioner has proposed a feeding restriction. Pea vines/forage can be included in beef cattle diets up to 35% and up to 50% of

dairy cattle diets for potential dietary burdens of 0.98 and 1.4 ppm, respectively. Pea hay [88% DM] can be up to 25% in beef cattle diets and up to 60% of dairy cattle diets.

From the feed items in this petition and co-pending petition, 3F4268, all of the feed items in cattle diets can be treated with quizalofop ethyl ester. A theoretical beef cattle diet consisting of canola meal, bean and pea forage, pea hay, and sugarbeet tops which none-the-less maximizes the potential quizalofop exposure of 2.1 ppm. A theoretical dairy cattle diet consisting of pea and bean forage would none-the-less maximize the potential quizalofop exposure at 2.4 ppm. Substitutions of other feed items and varying their percentages in the diets would give a lower dietary quizalofop burden.

The results of the quizalofop ethyl ester bovine feeding study show that finite residues will actually occur in milk and tissues from the feeding of quizalofop ethyl ester treated racs or their processed feed items when Assure® II is used as directed. The established quizalofop and quizalofop ethyl ester tolerance in milk, and in fat, meat, and meat by-products of cattle, goats, hogs, horse, and sheep are adequate and need not be increased from these additional uses.

POULTRY

A poultry feeding study has been submitted and reviewed (ibid). In summary, 3 groups of 20 hens (plus one control group) were dosed encapsulated at 0.1, 0.5, and 5 ppm of quizalofop ethyl ester daily for 28 consecutive days. Eggs were collected daily and after 28 days 3/4 of the hens in each test group were sacrificed and samples of fat, liver, kidney, breast and thigh muscles were collected and analyzed. Tissues from each test group were pooled prior to analysis. The remaining 5 hens were fed a regular poultry diet without quizalofop ethyl ester for an additional 7 days before sacrifice. No quizalofop residues were detected in the liver to <0.05 ppm, and in breast and thigh muscles to <0.02 ppm for any dose administered. From the 5 ppm dose, one kidney sample showed 0.09 ppm quizalofop, 2 fat samples were 0.05 and 0.06 ppm quizalofop, and one egg sample was 0.02 ppm quizalofop.

Poultry feed item in this petition is canola meal at 15% of the diet with a potential poultry dietary burden from the feed item at 0.1 ppm based on the CBTS suggested tolerance.

The results of the quizalofop ethyl ester poultry feeding study show that while it is not possible to establish with certainty whether finite residues will actually occur in eggs and tissues from the feeding of quizalofop ethyl ester treated racs or their processed feed items when Assure® II is used as directed, there is a reasonable expectation for such residues to occur. The established tolerance of quizalofop and quizalofop ethyl ester in eggs, and in fat, meat, and meat by-products of poultry are adequate and need not be changed from these addition-al uses.

HARMONIZATION OF TOLERANCES

An INTERNATIONAL RESIDUE LIMIT STATUS SHEET (IRL) is attached to this review. Since there are no Mexican or Codex MRLs/toleranc-es, compatibility is not a problem at this time. Compatibility cannot be achieved with the Canadian negligible residue type limit at 0.1 ppm as the USA use pattern had findings of real residues above 0.1 ppm.

cc:R.F.,Circu,Reviewer(FDG),PP#5F4545.
7509C:CBTS:Reviewer(FDG):CM#2:Rm804Q:305-5826:FDG:2/9/96:edit:fdg:2/21/96.
RDI:TPT-1:2/13/96:BrSrSci:RALoranger:2/20/96:ActBrCh:EZager:2/20/96.

MEMORANDUM

Subject: **PP# 5F4545/FAP# 6H5737 - QUIZALOFOP ETHYL ESTER (ASSURE®) ON THE FOLIAGE OF LEGUME VEGETABLES (EXCEPT SOYBEANS) CROP GROUP, CANOLA AND CANOLA PROCESSED COMMODITIES.**
Review of May 23, 1996, Amendment.
Chemical No. 128711
(No MRID #){DP Barcode D226692}

From: Francis D. Griffith, Jr., Chemist
Chemistry Branch I - Tolerance Support

To: D. McCall, Acting Section Head
Risk Characterization and Analysis Branch

Thru: E. Zager, Acting Chief
Chemistry Branch I - Tolerance Support

INTRODUCTION

E.I. duPont de Nemours and Company, Agricultural Products, in a letter dated May 23, 1996, signed by T.E. Catika submitted an amendment deleting proposed uses for Assure® (quizalofop ethyl ester) from all crops except canola and proposed revised tolerances for only canola seed and canola meal. This amendment was submitted in response to deficiencies noted in our 21 Feb 96 review by F. Griffith (qv). Our conclusions and recommendation follow.

EXECUTIVE SUMMARY OF RESIDUE CHEMISTRY DEFICIENCIES

- NONE -

RECOMMENDATION

CBTS recommends for the requested permanent tolerances for the combined residues of the herbicide quizalofop-p ethyl ester and the acid, all expressed as quizalofop ethyl ester in or on canola seed 1 ppm, and the Section 701 MRL for canola meal at 1.5 ppm.

A DRES analysis may be initiated using the CBTS suggested revised total quizalofop ethyl ester tolerances on canola seed at 1 ppm and canola meal at 1.5 ppm. There is no anticipated concentration of quizalofop ethyl in canola oil. There is no anticipated change in the secondary tolerances for quizalofop-ethyl in meat, milk, poultry, and eggs from the use of the additional quizalofop-ethyl treated feedstuffs. The DRES analysis should use these values.

CONCLUSIONS

1. CBTS Conclusion on **Directions for Use**

CBTS reiterates the petitioner has proposed an adequate set of directions for use of quizalofop-ethyl ester, formulated as Assure®, in conjunction with an approved oil concentrate, or a non-ionic surfactant on canola and crambie.

2. CBTS Conclusion on the **Residue Analytical Method**

CBTS reiterates that the results of the successful TMV is not a prerequisite for a tolerance on canola and canola processing commodities as there is already an enforcement method in PAM-II.

3. CBTS Conclusion on **Magnitude of the Residue - Crop Field Trials**

The petitioner presented a revised section F proposing a quizalofop-ethyl ester tolerance on canola seed at 1 ppm. The petitioner withdrew the proposed quizalofop-ethyl ester tolerance for foliage of legume vegetables from this petition.

The deficiencies 8b, 8e, and 8f are resolved.

4. CBTS Conclusion on **Magnitude of the Residue - Processed Food/ Feed**

The petitioner has conducted an adequate canola processing study using canola bearing detectable residues following a single 6X exaggerated application with a 45-day PHI. Total quizalofop residues were shown to concentrate only in canola meal. Residues declined in canola oil. The petitioner presented a revised Section F proposing a total quizalofop Section 701 Maximum Residue Limit (MRL) on canola meal at 1.5 ppm, and deleting the proposed total quizalofop ethyl tolerances for canola oil. Deficiency 9 is resolved.

DETAILED CONSIDERATIONS

DIRECTIONS FOR USE

CBTS reiterates the petitioner has proposed an adequate set of directions for use of quizalofop-ethyl ester, formulated as Assure®, in conjunction with an approved oil concentrate, or a non-ionic surfactant on canola and crambie.

RESIDUE ANALYTICAL METHOD

CBTS reiterates that the revised residue analytical method for quizalofop-p and its acid metabolite as presented in PP# 3F4268; ie, LAN-1, has been submitted for a Tolerance Method Validation (TMV) in EPA laboratories. The Analytical Chemistry Branch (ACB) noted several deficiencies in the method (see memoranda by H. Hundley dated 1 July 95). The petitioner needs to respond to ACB's concerns with a revised method before we can get the TMV back on track. CBTS reiterates that the results of the successful TMV is not a prerequisite for a tolerance on canola and canola processing commodities. There is already an adequate enforcement method for quizalofop-ethyl ester in PAM-II.

MAGNITUDE OF THE RESIDUE - CROP FIELD TRIALS

DEFICIENCIES

8b. CBTS concludes that quizalofop and its metabolites, all expressed as quizalofop-p ethyl ester, are not expected to exceed the proposed 2 ppm tolerance on canola when Assure® II plus the surfactant are used as directed. However, this tolerance is higher than necessary (see conclusion 8f below).

8f. Since CBTS recommends for tolerances no higher then necessary, the petitioner will need to submit a revised section F proposing total quizalofop-ethyl ester tolerances for canola at 1 ppm for 40 CFR §180.441(a) and for the foliage of legume vegetables subgroup foliage of legume vegetables (except soybeans) at 0.5 ppm for 40 CFR §180.441 (c).

PETITIONER'S RESPONSE

The petitioner presented a revised section F proposing a quizalofop-ethyl ester tolerance on canola seed at 1 ppm.

The petitioner withdrew the proposed quizalofop-ethyl ester tolerance for foliage of legume vegetables from this petition.

CBTS COMMENTS

The deficiencies are resolved.

MAGNITUDE OF THE RESIDUE - PROCESSED FOOD/FEED

DEFICIENCY

The petitioner has conducted an adequate canola processing study using canola bearing detectable residues following a single 6X exaggerated application with a 45 day PHI. Total quizalofop residues were shown to concentrate only in canola meal. Residues declined in canola oil. In a revised Section F the petitioner will need to propose a total quizalofop-ethyl ester Section 701 Maximum Residue Limit (MRL) on canola meal at 1.5 ppm. The petitioner needs to delete the proposed total quizalofop-ethyl ester tolerances for canola oil in the revised section F.

PETITIONER'S RESPONSE

The petitioner presented a revised section F proposing a quizalofop-ethyl ester maximum residue limit on canola meal at 1.5 ppm.

The petitioner withdrew the proposed quizalofop-ethyl tolerance for canola oil.

CBTS COMMENTS

Deficiency 9 is resolved.

cc:R.F.Taylor[PM-19,HFB/RD]R.F.,Circu,Reviewer(FDG),PP#5F4545.
7509C:CBTS:Reviewer(FDG):CM#2:Rm804Q:305-5826:FDG:6//96:edit:fdg:6/14/96.
RDI:TPT-1:6/13/96:BrSrSci:RALoranger:6/13/96:ActBrCh:EZager:6/14/96.

Attachment 3. Memorandum of S. Knizner, 5/14/96, PP#6E4652

MEMORANDUM

DATE: 5/14/96

SUBJECT: **Quizalofop-ethyl - PP#6E4652.** IR-4 Petition for Tolerance in/on Mint.

DP Code: D223397 Priority: 6
Reg #: 352-541 Trade Name: Assure II
Chem #: 128711 40 CFR: 180.441
Caswell: 215D MRID #: 43917301

TO: Hoyt Jamerson, PM Team 43
ERMUS/RSB
Registration Division (7505W)

FROM: Steven Knizner, SanYvette Williams-Foy, Tina Manville
Pilot Interdisciplinary Risk Assessment Team
RCAB/HED (7509C)

THRU: Michael Metzger, Acting Chief
RCAB/HED (7509C)

INTRODUCTION

IR-4, on behalf of the Oregon Agricultural Experiment Station, requests the establishment of a tolerance for the combined residues of the herbicide quizalofop-p ethyl ester (ethyl(R)-2-[4-((6-chloroquinoxalin-2-yl)oxy)phenoxy] propionate), and the S enantiomers of the ester and the acid, all expressed as quizalofop-p ethyl ester, in or on the raw agricultural commodity mint at 3 ppm. Three Section 18 Specific Exemptions (WA, OR and MT) were granted in 1993 for the use of quizalofop-ethyl on mint.

RECOMMENDATION

Provided the petitioner **revises Section F of the tolerance petition to request establishment of a 2 ppm tolerance** for the combined residues of the herbicide quizalofop-p ethyl ester, and the S enantiomers of the ester and the acid, all expressed as quizalofop-p ethyl ester, in or on the raw agricultural commodities **peppermint, tops** and **spearmint, tops**, HED has no objections to the establishment of this tolerance. Dietary exposure risk estimates do not exceed HED's level of concern.

CONCLUSIONS

Hazard Assessment

In conjunction with the review of PP#5F4545 (petition for quizalofop-ethyl tolerances in/on foliage of legume vegetables and canola seed and processed commodities), TOX concluded that the current database for quizalofop-ethyl was adequate (W. Phang, 2/26/96, D220477,

D220479, D220481, see Attachment 1). That review went on to state that the RfD is 0.009 mg/kg/day. The RfD was established based on the results of the chronic feeding/oncogenicity study in rats (with a NOEL of 0.9 mg/kg/day and an uncertainty factor of 100). The Cancer Peer Review Committee has evaluated the data on the incidence of liver tumors found in the mouse oncogenicity study, and the same data were considered by the Science Advisory Panel. It was concluded that quizalofop-ethyl would probably be best classified as a Category "D" carcinogen (not classifiable as to human carcinogenicity). No acute dietary endpoints have been identified.

Dietary Exposure

1. CBTS has previously concluded that the nature of the quizalofop-p ethyl ester residue in plants is adequately understood based on metabolism studies in cottonseed, potatoes, soybeans, tomatoes and sugarbeets. The residues of concern are quizalofop-p ethyl ester and its acid metabolite, quizalofop-p, and the S enantiomers of both the ester and the acid, all expressed as quizalofop-p ethyl ester (F.Griffith, 2/21/96, PP# 5F4545/FAP# 6H5737). We consider it appropriate to translate these data to mint.

2. Method I in PAM II (DuPont Method AMR-153-83, rev. 3) is an adequate enforcement method for determination of quizalofop-p-ethyl ester and related regulated residues in mint.

3. **Adequate residue data were provided to support a tolerance of 2.0 ppm.** Section F of the petition should be modified to reflect this tolerance level. Additionally, in order to conform to the racs listed in Subdivision O, Table II (September, 1995), Section F should be modified to request tolerances for **Peppermint, tops** and **Spearmint, tops**.

4. Processing data provided indicate no concentration of residues in mint oil. No food additive tolerances are required for mint oil. There are no Delaney considerations associated with this tolerance petition.

5. Secondary residues are not expected in animal commodities as no feed items are associated with the proposed use in/on mint.

6. A DRES analysis was recently conducted (B.Steinwand, 3/7/96, "Dietary Exposure Analysis for Quizalofop ethyl in/on Legumes, Sugarbeets, and Soybeans"). For purposes of the current analysis, the "new" tolerances listed in the previous analysis were changed to pending status. Corrections to the database used in the 3/7/96 analysis included: 1) removal of carob, peanuts (whole) and peanut oil, which were inadvertently listed as new uses under PP#3F4268; and 2) residue levels for soybean flour were set at 0.5 ppm (instead of 0.7 ppm) in accordance with directions given in the CBTS memo dated 10/6/95 (F.Griffith, CBTS #16261, D219638).

   a. Acute Dietary Risk. Because no acute dietary risk endpoints were identified, this analysis was not conducted.

   b. Chronic Dietary Risk. A DRES chronic dietary risk analysis was performed using a worst case estimate of tolerance level residues and the assumption of 100% crop treated to calculate the TMRC for the US general population and 22 subgroups. Summaries of the TMRCs and their representations as percentages of the RfD are included in Attachment 2.

   - US Population - Existing and pending tolerances result in a TMRC of 4.63×10^{-4} mg/kg/day, which represents 5.14% of the RfD for the US general population (48 states). The proposed use will add a TMRC of 2×10^{-6} mg/kg/day, which represents 0.016% of the RfD. The TMRC for the combined total (existing and pending tolerances + proposed use) will be 4.64×10^{-4} mg/kg/day, which will occupy 5.15% of the RfD.

   - Highest Exposed Population Subgroup - Existing and pending tolerances (see Appendix Table III) result in a TMRC of 1.7×10^{-3} mg/kg/day, which represents 18.5% of the RfD for the highest exposed population subgroup, Non-nursing infants (<1 year old). The proposed use will not contribute to the dietary burden of this population subgroup.

   Based on the risk estimates calculated, dietary exposure does not exceed HED's level of concern.

   c. Dietary Cancer Risk. Because quizalofop ethyl is classified as a Category "D" carcinogen (not classifiable as to human carcinogenicity) dietary cancer risk was not estimated.

   d. Anticipated Residues. Because the existing and pending tolerances plus the proposed use do not result in TMRCs that exceed the RfD for the US general population or any of the 22 subgroups analyzed, there is no need for anticipated residue assessment refinement.

DETAILED CONSIDERATIONS

DIETARY EXPOSURE

Residue Data

Table 1. Residue Consideration Summary Table

PARAMETER	RESIDUE DATA
CHEMICAL	Quizalofop-ethyl
FORMULATION	EC - Assure II Herbicide (10.3% quizalofop-ethyl by weight as ai)
CROP	Peppermint and Spearmint
TYPE APPLICATION	Ground
# APPLICATIONS	Maximum of 2
TIMING	When weeds (quackgrass, green foxtail, volunteer cereals, and/or wild oats) are from 2 to 10 inches tall.
RATE/APPLICATION	0.10 to 0.20 lbs ai/A
RATE/SEASON	0.20 lbs ai/A/season
RESTRICTIONS	Do not apply this product within 30 days of harvest. Do not apply through any type of irrigation system. Do not graze animals on green forage or stubble. Do not utilize hay or straw for animal feed or bedding. Use a minimum of 15 gallons of water per acre. Do not exceed 40 gallons of water per acre. Apply with ground equipment. Always include a spray adjuvant (petroleum based at 1.0% v/v or nonionic surfactant at 0.25% v/v).
RESIDUE DATA SOURCE	IR-4 (MRID #43917301)
FIELD TRIAL LOCATIONS	IN (1) - peppermint; OR (1) - peppermint; WA (1) - spearmint (see Note to PM following this Table)
SAMPLE HANDLING/ PROCESSING	Fresh "hay" samples were harvested either by hand, or by using a Swift flail harvester, or a mint chopper. All "hay" samples were immediately frozen and maintained frozen (<-10 C) until analysis. PIRAT notes that the samples designated "hay" actually correspond to the rac listed for peppermint and spearmint in Subdivision O, Table II (September 1995), which is "tops (leaves and stems)". Samples used for processing into oil were distilled from fresh hay the same day as harvest in the OR and WA trials (using small mint stills). For the IN trial, hay was air dried on a greenhouse bench for 15 days then water distilled.
PERFORMING LAB	Enviro-Test Laboratories, Edmonton, Alberta, Canada
ANALYTICAL METHOD	Analytical Method for the Quantification of Quizalofop (IN-YE945) and Quizalofop-Ethyl (DPX-79379) in Raw and Processed Agricultural Commodities (HPLC/UV) (MRID #43917301).
METHOD VALIDATION RESULTS	The analytical method was adequately validated using rac and oil samples fortified at various levels (from 0.05 to 0.5 ppm) with quizalofop-p ethyl ester and quizalofop acid. Recoveries were in the range considered acceptable by the Agency (69 to 121%, average recovery 99% $\pm$ 17%). Adequate representative chromatograms were presented.
FIELD TRIALS	Trials were conducted in 1990 in IN (1), OR (1), and WA (1). Each location consisted of one or two untreated control plots, two plots treated at 0.2 lb ai/A and two plots at 0.4 lb ai/A. One application was made, using ground equipment and a surfactant. Samples were harvested with either a 30 or 45 day PHI. In the OR and WA trials, oil samples were distilled the day of harvest using small vapor stills. In the IN trial, samples for oil were air dried 15 days, distilled in boiling water and then frozen. All samples were stored frozen (<-10 C or lower) until analysis. Field trial samples were stored frozen for a maximum of 654 days from harvest to analysis.

Table 1. Residue Consideration Summary Table

PARAMETER	RESIDUE DATA
RESIDUE DATA (RAC)	For the proposed maximal seasonal label rate of 0.2 lb ai/A and the proposed 30 day PHI, combined regulated residues ranged from 0.06 to 1.0 ppm in/on fresh mint hay. Residue data are summarized below in Table 2.
RESIDUE DATA (PROCESSING STUDY)	All residues in mint oil produced from mint treated at either 0.2 or 0.4 lb ai/A and 30 day PHI were nondetectable (<0.05 ppm).
STORAGE STABILITY	Adequate data were presented to demonstrate that quizalofop ethyl ester and quizalofop acid were stable in mint hay and mint oil after up to approximately 600 days of frozen storage. These data are adequate to support the sample storage intervals in this study.
CODEX	There are no CODEX, Canadian, or Mexican MRLs for quizalofop-ethyl residues in/on mint.

NOTE to PM: Although current Chemistry Guidelines (see Pesticide Reregistration Rejection Rate Analysis Residue Chemistry Follow-up Guidance for Number and Location of Domestic Crop Field Trials, June 1994, EPA 738-K-94-001) require 5 field trials (3 in region 11 [WA, OR, ID] and 2 in region 5 [north-central US]). We note that the field trials for this study were conducted in 1990, prior to publication of the guidance. Because data are available for each location reflecting both a 1x and 2x maximum seasonal application rate scenario, PIRAT concludes that the number of field trials conducted is adequate in this case. However, for future mint tolerance petition submissions, IR-4 should be made aware of data requirements set forth in the guidance document.

Table 2. Summary of Field Trial Results.

Matrix	Applic. Rate (lb ai/A)	PHI (days)	Total Regulated Residues (ppm)		
			IN	OR	WA
tops	0.2 (1x rate)	30 (±2) (minimum PHI)	0.22	0.46	0.92
			0.06	0.38	1.0
	0.4	30 (±2)	0.35	1.0	2.6
			0.14	1.2	1.9
	0.2	45 (±3)	<0.05	0.14	0.21
			<0.05	0.22	0.35
	0.4	45 (±3)	<0.05	0.40	0.81
			0.06	0.42	0.64
oil	0.2	30 (±2)	<0.05	<0.05	<0.05
	0.4	30 (±2)	<0.05	<0.05	<0.05
	0.2	45 (±3)	<0.05	<0.05	<0.05
	0.4	45 (±3)	<0.05	<0.05	<0.05

Attachment 4. Chronic DRES Analysis 2/4/98 (note that this analysis does not include the contribution from canola - see text for details)