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Quizalofop Summary Document
Registration Review: Initial Docket
December 2007

Case Number 7215

Approved by: _____
Steven Bradbury, Ph.D.
Director
Special Review and Reregistration Division

Date: 11/29/07

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I. Preliminary Work Plan

Introduction:

The Food Quality Protection Act of 1996 mandated a new program: registration review. All pesticides distributed and sold in the United States must be registered by the EPA, based on scientific data showing that they will not cause unreasonable risks to human health, workers or the environment when used as directed on the product label. The new registration review program is intended to ensure that as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects. Changes in science, public policy, and pesticide use practices will occur over time. Through the new registration review program, the Agency periodically reevaluates pesticides make sure that as the change occurs, products in the marketplace can be used safely. Information on this program is provided at the following website: http://www.epa.gov/oppsrrd1/registration_review/.

The Agency has begun to implement the new Registration Review program and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. The public phase of registration review begins when the initial docket is opened for each case. The docket is the Agency's opportunity to state what is knows about the pesticide and what additional risk analyses and data or other information it believes are needed to make a registration review decision. After reviewing and responding to comments and data received in the docket during this initial comment period, the Agency will develop and commit to a final work plan and schedule for the registration review of quizalofop.

Quizalofop is a selective post-emergence herbicide used on a number of food and feed crops. It was registered for use in the late 1980's. Quizalofop-ethyl is a 50/50 racemic mixture of R- and S-enantiomers. Quizalofop-p-ethyl is the purified R-enantiomer and the pesticidally active isomer.

Anticipated Risk Assessment and Data Needs:

The Agency anticipates conducting comprehensive human health and ecological risk assessments, including an endangered species assessment, for all uses of quizalofop.

Ecological Risk:

- New ecological risk assessments for all registered uses were conducted in October 2005. However, the Agency has not conducted a risk assessment that supports a complete endangered species determination for quizalofop-ethyl or quizalofop-p-ethyl and a complete assessment will be conducted for registration review. Please refer to Section III, Ecological Risk Assessment Problem Formulation, for a detailed discussion of the anticipated risk assessment needs.

- There are two chronic avian studies, which have been submitted. If upon further review, these studies do not provide useful information on the reproductive effect of quizalofop in birds, new studies will be required.

- The Agency anticipates needing the following data in order to conduct a complete ecological risk assessment, including an endangered species assessment, for all uses:
    - (GLN 850.4225) Seedling emergence (Tier 2) for quizalofop-p-ethyl.
    - (GLN 850.4250) Vegetative vigor (Tier 2) for quizalofop-p-ethyl.
    - (GLN 850.1350) Chronic early life-cycle toxicity studies for estuarine marine invertebrates for quizalofop-p-ethyl.

- The planned ecological risk assessment will allow the Agency to determine whether quizalofop use has "no effect" or "may affect" federally listed threatened or endangered species (listed species) or their designated critical habitat. If the assessment indicates that quizalofop "may affect" a listed species or its designated critical habitat, the assessment will be refined to determine whether use of quizalofop is "likely to adversely affect" the species or critical habitat or "not likely to adversely affect" the species or critical habitat. When an assessment concludes that a pesticide's use "may affect" a listed species or its designated critical habitat, the Agency will consult with the U.S. Fish and Wildlife Service and/or National Marine Fisheries Service (Services), as appropriate.

Human Health Risk:

- The current dietary risk assessment for quizalofop-ethyl was conducted according to Agency policy and results in no risks of concern. Because the toxicological profile of quizalofop-ethyl and quizalofop-p-ethyl are sufficiently similar, the Agency has determined the currently available toxicity data on quizalofop-ethyl are adequate to support risk assessments reflecting uses of both quizalofop-ethyl and quizalofop-p-ethyl. Although occupational risk assessments have not been completed for all uses, no dermal or inhalation endpoints have been selected because quizalofop-p-ethyl and quizalofop-ethyl do not appear to be toxic via dermal and inhalation routes of exposure. Based on existing risk assessments, occupational exposure risk appear to well below the Agency's level of concern (LOC). Therefore, additional assessments are not needed.

- The Agency anticipates no revisions to the human health risk assessments. No new human health data are required.

Timeline:

EPA has created the following estimated timeline for the completion of the quizalofop registration review.

Activities	Estimated Month/Year
Phase 1: Opening the Docket	
Open Public Comment Period for Quizalofop Docket	2007– Dec.
Close Public Comment Period	2008– Mar.
Phase 2: Case Development	
Final Work Plan (FWP)	2008– May-July
Issue DCI	2009– Mar.-May
Data Submission	2011– Mar.-May
Preliminary Risk Assessment & Public Comment	2012– Sep.-Nov.
Close Public Comment Period	2012– Nov.-Jan.
Phase 3: Registration Review Decision	
Open Public Comment Period for Proposed Reg. Review Decision	2013– Feb.-Apr.
Close Public Comment Period	2013– Apr.-Jun.
Final Decision and Begin Post-Decision Follow-up	2013
Total	6 years

Guidance for Commenters

The public is invited to comment on EPA's preliminary registration review work plan and rationale. The Agency will carefully consider all comments as well as any additional information or data provided prior to issuing a final work plan for quizalofop.

Through the registration review process, the Agency intends to solicit information on trade irritants and, to the extent feasible, take steps toward facilitating irritant resolution. Growers and other stakeholders are asked to comment on any trade irritant issues resulting from lack of Maximum Residue Limits (MRLs) or disparities between U.S. tolerances and MRLs in key export markets, providing as much specificity as possible regarding the nature of the concern. There are 44 U.S. tolerances for quizalofop-p-ethyl and quizalofop-ethyl, but not all of these tolerances have been harmonized with MRLs at this time. Tolerances on animal commodities have been harmonized with Canada. Other tolerances have not been harmonized, but allowable residue levels are similar. Please refer to Section IV of this document, Human Health Effects Scoping Document, for a detailed comparison of MRLs.

Quizalofop is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act, based on information provided at http://oaspub.epa.gov/tmdl/waters_list.impairments?p_impid=3. The Agency invites submission of water quality data for this pesticide. To the extent possible, data should conform to the quality standards in Appendix A of the "OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process" (see: http://www.epa.gov/oppfead1/cb/ppdc/2006/november06/session1-sop.pdf), in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To help address potential environmental justice issues, the Agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical or unusually high exposure to quizalofop, compared to the general population. Please comment if you are aware of any sub-populations that may have atypical or unusually high exposure compared to the general population.

Stakeholders are also specifically asked to provide information and data that will assist the Agency in refining the ecological risk assessment, including any species-specific effects determinations.

The Agency is interested in receiving the following information:

1. confirmation on the following label information
    a. sites of application
    b. formulations
    c. application methods and equipment
    d. maximum application rates in units related to mass per unit area of treatment zone
    e. frequency of application, application intervals, and maximum number of applications per season
    f. geographic limitations on use
2. use or potential use distribution (e.g., acreage and geographical distribution of relevant crops)
3. use history
4. median and 90^{th} percentile reported use rates (lbs ai/acre) from usage data – national, state, and county
5. application timing (date of first application and application intervals) by crop – national, state, and county
6. sub-county crop location data
7. usage/use information for non-agricultural uses (e.g., forestry, residential, rights-of-way)
8. directly acquired county-level usage data (not derived from state level data)
    a. maximum reported use rate (lbs ai/acre) from usage data – county
    b. percent crop treated – county
    c. median and 90^{th} percentile number of applications – county
    d. total pounds per year – county
    e. the year the pesticide was last used in the county/sub-county area
    f. the years in which the pesticide was applied in the county/sub-county area
9. typical interval (days)
10. state or local use restrictions
11. ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency
12. monitoring data

Next Steps:

After the comment period closes, the Agency will review any comments received, and then issue a Final Work Plan for this pesticide.

II. Fact Sheet

The Quizalofop Registration Review Case (#7215) includes two active ingredients:

1. **Quizalofop-p-ethyl**
2. **Quizalofop-ethyl**

Background Information:

- **Quizalofop-p-ethyl** is part of Registration Review case number: 7215
- Quizalofop-p-ethyl PC Code: 128709 CAS#: 100646-51-3
- Technical registrants:
  - E.I. Du Pont De Nemours Co., Inc. (Company No. 352)
  - Nissan Chemical Industries Ltd. (Company No. 33906)
- First approved for use in a registered product in 1990.
- Not subject to reregistration (no Reregistration Eligibility Decision [RED]).
- There are six FIFRA section 3 registrations and four FIFRA section 24(c) special local need registrations

- **Quizalofop-ethyl** is part of Registration Review case number: 7215
- Quizalofop-ethyl PC Code: 128711 CAS#: 76578-14-8
- Technical registrant:
  - E.I. Du Pont De Nemours and Co., Inc. (Company No. 352)
- First approved for use in a registered product in 1988, however all end use product registrations have been cancelled prior to 1996.
- No current active end-use products. One active technical registration.

- Quizalofop-ethyl is a 50/50 racemic mixture of R- and S-enantiomers. Quizalofop-p-ethyl is the purified R-enantiomer and the pesticidally active isomer. Because the toxicological profile of the 50/50 racemic mixture (quizalofop-ethyl) and the R-enantiomer (quizalofop-p-ethyl) are sufficiently similar, the Agency has determined that the currently available toxicity data on quizalofop-ethyl are adequate to support risk assessments reflecting uses of both quizalofop-ethyl and quizalofop-p-ethyl (the R-enantiomer).

- Special Review and Reregistration Division Chemical Review Manager (CRM): Rusty Wasem: wasem.russell@epa.gov.
- Registration Division Product Manager (PM):
  James Tompkins: tompkins.james@epa.gov.

Use & Usage Information:

(For additional details, please refer to the BEAD Appendix A document in the quizalofop docket.)

- **Quizalofop** is a selective postemergence herbicide that is used to control annual and perennial grasses, excluding sedges and broadleaf weeds.
- Quizalofop is used on food, feed, seed, and for other non-food/non-feed uses. Food, feed, and seed uses include the following: grains, legumes, cotton, garlic, mint, soybean, sugar beets, sunflower, pineapple, and Chinese cabbage. Non-food/non-feed uses include: cottonwood and poplar plantations, and uncultivated areas such as fencerows and roadsides.
- There are no residential uses.
- Application methods:
    - ground (broadcast, band, or soot spray), or aerial
    - post-emergence of weeds
- Greatest poundage of quizalofop is used on soybeans.
- Approximately 30% of mint and 10% of canola/rapeseed, dry beans/peas, and garlic crops are treated with quizalofop(according to SLUA).

Recent Actions:

- In October 2005, Drinking water exposure for quizalofop-p-ethyl (TARGA™) on proposed and registered uses were completed.
- In October 2005, Environmental Fate and Effects Division (EFED) risk assessments were completed.
- In August 2006, Health Effects Division (HED) human health risk assessments were completed.
- In November 2006, Section 3 new use registration request for quizalofop-p-ethyl (TARGA™) on sunflowers, flax, wheat and barley were approved.

Ecological Risk Assessment Status:

The following ecological outcomes are anticipated based on the limited data and risk assessments currently available. Please refer to Section III, Ecological Risk Assessment Problem Formulation, for a detailed discussion of the anticipated ecological risk assessment needs. A summary follows:

- Risks are unlikely to exceed the Agency's LOC for listed and non-listed species for: acute risks to aquatic invertebrates, aquatic plants, birds, fish, mammals, terrestrial invertebrates.

- Risks are unlikely to exceed the Agency's LOC for listed and non-listed species for: chronic risks to aquatic plants, birds, fish, and terrestrial invertebrates.
- Risks are likely to exceed the Agency's LOC for listed and non-listed species for chronic risks to mammals.
- Acute and chronic risks to non-target terrestrial plants have not been assessed, but are expected to exceed the Agency's LOC.
- Uncertainty exists for chronic risks to aquatic invertebrates, since the Agency has no chronic toxicity data for risk assessment. These data are required for estuarine invertebrates since estuarine animals seem to be more sensitive than freshwater animals in acute toxicity tests.

Human Health Risk Assessment Status:

Please refer to Section IV, Human Health Effects Scoping Document, for a detailed discussion of the anticipated risk assessment needs for human health. A summary follows:

Dietary (Food and Water):

- Acute dietary risk assessments for quizalofop-p-ethyl and quizalofop-ethyl were deemed unnecessary because no toxic endpoint attributable to a single oral dose has been identified. Therefore, no acute dietary assessment has been conducted.
- Chronic dietary risk assessments for quizalofop-p-ethyl and quizalofop-ethyl are conservative and unrefined with risks below the Agency's LOC because the dietary analysis was based on tolerance level residues.
- There are no dietary risks for quizalofop-p-ethyl and quizalofop-ethyl that exceed the Agency's LOC.

Residential:

- There are no residential uses of quizalofop-p-ethyl and quizalofop-ethyl.

Occupational:

- An occupational assessment was conducted for quizalofop-p-ethyl for the proposed uses on barley, flax, sunflower and wheat in 2006.
- Risk estimates based on inhalation exposures of pesticides handlers and applicators for quizalofop-ethyl for barley, flax, sunflower, wheat, cotton, pineapple, and non-crop areas are below the Agency's LOC.
- Occupational assessments are not necessary for quizalofop-ethyl because there is only a technical registration.

Tolerances:

- The following is a summary of tolerances for quizalofop-p-ethyl according to CFR §180.441.
    - quizalofop-ethyl
        - 36 tolerances
    - quizalofop-p-ethyl
        - 7 tolerances
        - 1 tolerance (regional)

Data Call-In Status:

- A DCI has not been issued for quizalofop-p-ethyl or quizalofop-ethyl.
- DCI(s) will be issued for quizalofop during the registration review process.

Labels:

A list of registration numbers may be found in the docket and the labels for quizalofop-p-ethyl and quizalofop-ethyl can then be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlabl/ppls.home.

U. S. ENVIRONMENTAL PROTECTION AGENCY
Washington, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: November 1, 2007

MEMORANDUM

Subject: EFED Problem Formulation for Quizalofop-p-ethyl Registration Review
PC Code: **Quizalofop-ethyl** (PC 128711) and **Quizalofop-p-ethyl** (PC 128709)
DP Barcode: D344060, D544156

To: Russell Wasem, Chemical Review Manager
Laura Parsons, Risk Manager
Special Review and Reregistration Division (7508P)

From: Marie Janson, Environmental Scientist, ERBI
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11/30/7

Attached is the EFED's problem formulation document in support of the quizalofop-p-ethyl registration review docket opening. This memorandum outlines (1) the methods that will likely be used in the ecological risk assessment of quizalofop-p-ethyl (2) data gaps, and (3) additional data needs.

EXECUTIVE SUMMARY

Quizalofop-ethyl (including its R-enantiomer, quizalofop-p-ethyl) is a systemic herbicide that is rapidly absorbed by treated foliage and translocated to the roots and other growing points of the plant. Affected plant tissues become necrotic/chlorotic and die leaving treated plants stunted and non-competitive. It controls annual and perennial grasses. It can be applied using ground boom equipment, fixed wing aircraft as broadcast and banded applications, airblast and soil injection treatment applications. It is normally applied at low rates.

Currently, only products containing quizalofop-p-ethyl are registered. There are no active registered products containing quizalofop-ethyl. Quizalofop-ethyl is a 50/50 racemic mixture of R- and S-enantiomers. Quizalofop-p-ethyl is the purified R-enantiomer. The pesticidally active isomer is the R-enantiomer (quizalofop-p-ethyl).

Quizalofop-ethyl and quizalofop-p-ethyl (the R-enantiomer) were first registered in 1988. As a result, they were not subject to review under the re-registration process recently completed under FIFRA and FQPA as of August 3, 2006 for chemicals registered prior to 1984. Consequently, neither a Re-registration Eligibility Decision (RED) nor a Tolerance Re-registration Eligibility Decision (TRED) is available for the Registration Review process of these chemicals.

The most recent EFED risk assessments were completed in October 28, 2005, which reflect current registrations and uses of quizalofop-ethyl and quizalofop-p-ethyl. Based on the results of those assessments, the following risk concerns were noted:

- Chronic risks to listed and non-listed mammals
- Anticipated risks to listed and non-listed terrestrial plants
- Potential chronic risks to listed and non-listed estuarine/marine invertebrates. Since the toxicological profile of the 50/50 racemic mixture (quizalofop-ethyl) and the R-enantiomer (quizalofop-p-ethyl) are not complete, uncertainty exists for this assessment.

EFED anticipates revisions to the risk assessments based on new application scenarios and additional toxicity data requested. A new drinking water assessment may also be needed to address any new uses and/or application scenarios and to comply with new EFED guidelines.

Table 1 summarizes quizalofop-p-ethyl and quizalofop-ethyl submitted studies and studies that are requested to complete the toxicological profile.

Table 1 List of studies submitted and studies requested		
Studies submitted quizalofop-p-ethyl	**Studies submitted ** quizalofop-ethyl**	**Studies requested quizalofop-p-ethyl**
Seedling emergence (unacceptable)	Avian acute (mallard duck and bobwhite quail)	Seedling emergence based on TEP tier II
Vegetative vigor (unacceptable)	Avian dietary (mallard duck and bobwhite quail)	Vegetative vigor based on TEP tier II
Chronic bird (mallard duck and bobwhite quail)	Acute rat	Chronic estuarine marine invertebrate most sensitive species (mysid). No chronic freshwater or estuarine marine invertebrate studies were submitted therefore a chronic estuarine marine invertebrate study is requested to quantify risks. This data will also be used to estimate chronic values for freshwater invertebrates.
non- vascular aquatic plant study tier l green algae (*Selanastrum capricornutum)**	Acute freshwater fish (Rainbow trout and Bluegill)	
non- vascular aquatic plant study tier l blue green algae (*Anabaena flos-aquae*)	Acute freshwater aquatic invertebrate (daphnid)	
non- vascular aquatic plant study tier l estuarine marine diatom (*Skeletonema costatum*)	Acute estuarine marine fish (sheepshead minnow)	
non- vascular aquatic plant study tier l freshwater diatom (*Navicula pelliculosa*)	Acute estuarine marine aquatic invertebrate (mysid)	
vascular aquatic plant study tier 1 Duckweed (*lemna gibba)**	Chronic freshwater fish (fathead minnow)	
	Nontarget insects (honeybee)	

* Non vascular plant NOAEC values were not determined for quizalofop-p-ethyl. In the absence of those data, EFED based its risk estimation for non vascular plants on data from the NOAEC from the analog fenoxaprop-p-ethyl (27 ppb). It is understood that fenoxaprop-p-ethyl is more toxic to non vascular plants than quizalofop-p-ethyl (EC50 of 1770 ppb for quizalofop-p-ethyl vs 430 ppb for fenoxaprop -p-ethyl for Selanastrum capriconutum, the most sensitive species tested for both chemicals), and using data from fenoxaprop-p-ethyl may overestimate risk for quizalofop-p-ethyl. However, a chronic RQ of only 0.23 was observed when comparing the fenoxaprop-p-ethyl NOAEC of 27 ppb to the exposure data of quizalofop-p-ethyl at the highest application rate of 0.4125 lb ai/A

Therefore, although the above estimated values may not be complete substitutes for missing effects data, EFED is confident that listed species LOCs would not be triggered even if assessed with definitive NOAEC values. Thus, additional tier II toxicity data will not be requested at this time for non-vascular plants.
Estimated EECs for highest application rate of 0.4125 lb ai/A per season= 0.4125 lb ai/A/ 0.165lb ai/A=2.5 2.5x EEC 2.57 ppb (table#6) =6.425 ppb EECs for highest application rate. RQ=6.425 ppb/27 ppb NOAEC from fenoxaprop-p-ethyl =RQ 0.23
The NOAEC for *lemna gibba* however will be equal to the highest nominal concentration of 82.8 ppb.

** Additional studies for terrestrial and aquatic plants, chronic reproductive bird and chronic aquatic fish and invertebrates may be requested if quizalofop-ethyl is registered as an active labeled use.

PROBLEM FORMULATION

Problem formulation is used to establish the direction and scope of an ecological risk assessment. According to the Guidelines for Ecological Risk Assessment (USEPA, 1998), problem formulation consists of defining the problem and purpose for the assessment, and developing a plan for analyzing and characterizing risk. The critical components of the problem formulation are selection of the assessment endpoints, formulation of risk hypotheses and the conceptual model, and development of an analysis plan. The analysis plan and supporting rationale are aimed at determining whether the uses of quizalofop-p-ethyl and quizalofop-ethyl on Non-Food/Non-feed uses (alfalfa, beets, carrot (including tops), swiss chard, grasses grown for seed, cottonwood/poplar plantations, non-agricultural uncultivated areas/soils, onion, ornamental and or shade trees, radish spinach and for Food and Feed uses (agricultural fallow/idleland, barley, succulent and dried beans, snap beans, chinese cabbage, eucalyptus, canola, rape, cotton, crambe, flax, garlic, lentils, mint, peppermint and spearmint, dried and succulent peas, pineapple, soybeans, sugarbeets including tops, sunflower and wheat) could result in exposures that cause unreasonable adverse effects (risk) to non-target organisms including those federally listed as threatened or endangered (hereafter referred to as “listed”).

1. INTEGRATION OF AVAILABLE INFORMATION

The risk assessments available in the docket, and which serve as the basis for this problem formulation, include the following:

- October 28, 2005, Section 3 New use registration request for quizalofop-p-ethyl (TARGA^{TM}) on sunflowers, flax, wheat and barley (DP 310868)

- October 28, 2005, Drinking water exposure for quizalofop-p-ethyl (TARGA ^{TM}) on proposed and registered uses (DP 310868)

Risks, as identified in these assessments, are:

For mammals: Chronic risk to mammals, based on aerial and ground spray applications, occurred for the following crops:(1) sunflowers with a maximum seasonal rate of 0.12 lb ai /acre; (2) flax with a maximum seasonal rate of 0.165 lb ai /acre; and (3) wheat and barley with a maximum seasonal rate of 0.08 lb ai acre. Chronic RQs ranged from 1.14 to 3.54.

In addition, exceedences are anticipated for chronic risk to estuarine marine invertebrates with higher application rates. Terrestrial plants can not be assessed due to lack of acceptable data, however exceedences are anticipated for all modeled scenarios due to the chemical properties and mode of action of quizalofop-p-ethyl.

There are no reported incidents for 128711. There is only one incident for 128709 ref.# 1016677-001 which involved damage to some garden plants after they were exposed to spray drift of quizalofop-p-ethyl (Assure II) plus fomesafen sodium (Flexstar). Because the plants were exposed to two herbicides, it is uncertain which one or both caused the observed plant damage.

1. DATA GAPS AND ANTICIPATED DATA NEED

As mentioned above, the toxicological profile of the 50/50 racemic mixture (quizalofop-ethyl) and the R-enantiomer (quizalofop-p-ethyl) are not complete and the currently available toxicity data on quizalofop-ethyl are not adequate to support risk assessments reflecting uses of both quizalofop-ethyl and quizalofop-p-ethyl (the R-enantiomer). EFED will request additional data to complete the toxicological profile for quizalofop-ethyl and quizalofop-p-ethyl (the R-enantiomer).

Below is the preliminary identification of data gaps for the fate and ecological assessment:

Seedling emergence and vegetative vigor tests The terrestrial seedling emergence and vegetative vigor tests for plants exposed to quizalofop-p-ethyl that were submitted to the Agency in 1994 were classified as unacceptable. The Agency guidelines require that terrestrial plant toxicity testing for herbicides be performed using the typical end-use product (TEP). In addition, the above studies lack negative controls and insufficient information demonstrating that the concentration of acetone used in the study does not inhibit plant growth.
Decision: Seedling emergence and vegetative vigor studies based on TEP are requested for terrestrial seedling emergence and vegetative vigor tests for quizalofop-p-ethyl. Seedling Emergence (GLN 123-1a/850.4225) Vegetative Vigor (GLN 123-1b/850.4250)

Chronic estuarine/marine fish toxicity tests - The No Observable Adverse Effect Concentration (NOAEC) value of 33 ppb for estuarine/marine fish was estimated by applying the acute-to-chronic ratio (ACR)) from freshwater toxicity tests to the estuarine/marine acute toxicity values. In addition, no LOC exceedences occurred for chronic estuarine marine fish with RQs <0.01 for the 0.165 lb ai /A scenario. LOC exceedences are not anticipated for chronic estuarine marine fish with the higher application rate of 0.4125 lb ai/A per season.
Decision: Chronic estuarine/marine fish toxicity tests studies are not requested

Estuarine/marine invertebrate Early Life-Cycle toxicity data – No early life stage estuarine/marine invertebrate studies were submitted to the Agency. Estuarine marine invertebrates are the most sensitive aquatic organisms (mysid) exposed to quizalofop-ethyl. Since exceedences are expected from quizalofop-p ethyl and quizalofop-ethyl from many application scenarios, the early life-cycle estuarine marine invertebrate study for quizalofop-p-ethyl with mysid shrimp (most sensitive species tested) will be requested since no active labels exist for quizalofop-ethyl. However, if active labels occur for quizalofop-ethyl then additional studies for estuarine marine invertebrates would be requested.
Decision: Chronic early life-cycle estuarine/marine invertebrate toxicity tests studies with mysid (most sensitive species) conducted on quizalofop-p-ethyl are requested (GLN 72-4b/850.1350).

Freshwater invertebrates Early Life-Stage toxicity test - No early life-stage or full life-cycle chronic invertebrate studies were submitted for freshwater or estuarine marine invertebrates. However, based on ACRs derived from acute and chronic freshwater fish data, no exceedences would occur for chronic freshwater invertebrates exposed to quizalofop-ethyl.
Decision: An Early life-stage chronic freshwater invertebrate toxicity test for quizalofop-p-ethyl is not requested. Estimated values derived from ACRs will be sufficient.

Tier II study for non-vascular plant based on (*Selanastrum capricornutum)*
NOAECs were not determined for non-vascular plants exposed to quizalofop-p-ethyl to address listed species concerns and no studies were submitted for quizalofop-ethyl. A Tier II study which defines a NOAEC value would be beneficial in the definitive determination of risks to non-vascular plants. Risks to listed species are currently assessed using data from fenoxaprop-p-ethyl, a structural analog of quizalofop-p-ethyl. No LOCs exceedances were noted at the highest application rate of 0.4125 lb ai/A per season based on estimated EECs.
Decision: A Tier II study for non-vascular plants based on *Selanastrum capricornutum* for quizalofop-p-ethyl is not requested at this time. Data may be required for any future use with application rates higher than 0.4125 lb ai/A per season.

Environmental Fate Data and Sediment Toxicity Data for the degradate quizalofop acid:
Quizalofop-p-ethyl is anticipated to degrade quickly in soil to the major degradate, quizalofop acid. Previous assessments assume that quizalofop acid is the main species present in water, and that it is of equivalent toxicity as the parent. Furthermore, for exposure, this degradate was presumed to be stable via hydrolysis and photolysis, and in anaerobic environment (soil and water). With those assumptions, only chronic risks to listed and non-listed freshwater and estuarine marine invertebrates were anticipated, however not fully characterized due to lack of toxicity data.
Decision: Based on the current database for quizalofop-p-ethyl, environmental fate data for quizalofop acid are not required. However, if further assessment indicates toxicity and risks to aquatic organisms, those data may be requested for a refined risk characterization.

2. PESTICIDE TYPE, CLASS, AND MODE OF ACTION

Quizalofop-p-ethyl is a selective, post-emergence organic phenoxy herbicide that belongs to a subclass of phenoxy compounds known as Aryloxyphenoxys (fops). Quizalofop-p-ethyl is absorbed by the treated foliage and translocated to the roots and other growing points of the plant. Herbicides categorized as arloxyphenoxys have several modes of action which are as follows: (1) In terrestrial and aquatic vascular and nonvascular plants--- inhibition of acetyl CoA carboxylase (ACCase), a key enzyme in lipid biosynthesis; (2) In terrestrial and aquatic vascular and non-vascular plants-inhibition of cell mitosis or immediate termination of mitosis once exposure has been known to occur; (3) In terrestrial and aquatic vascular and non-vascular plants- inhibition of Acetyl-CoA carboxylase and the fatty acid synthesis pathway causes an inhibition of thylakoid membrane formation, chloroplast formation and multiplication, and finally a halt of cell membrane formation and cell division.

4. STRESSOR SOURCE AND DISTRIBUTION

The sources of the stressor considered are quizalofop -p-ethyl (PC Code 128709), quizalofop-ethyl (PC Code 128711), and quizalofop acid, the major degradate of concern.

Quizalofop-p-ethyl is stable to hydrolysis at pH's 5 and 7. Hydrolysis occurs at pH 9 with a half life of 2 days. Quizalofop-p-ethyl is stable to photolysis in water and soil. Acceptable aerobic soil metabolism study show that quizalofop-p-ethyl degrades with a half-life of 1 day to quizalofop acid and phenolic compounds. Quizalofop acid is considered to be the major exposure concern. Based on available fate studies, the acid is less persistent than the parent under aerobic conditions but more mobile than the parent compound. Its soil metabolism half lives in aerobic environment range from 4 to 8 weeks, depending on soil types. As for mobility, the mean adsorption K_{oc} of quizalofop acid is 476 (which is classified as moderately mobile), whereas the mean adsorption K_{oc} value of quizalofop-p-ethyl is 1816 (which is classified as slightly mobile). No additional environmental fate data are available for quizalofop acid.

As mentioned above, quizalofop-p-ethyl degrades quickly to form quizalofop acid, the major concern of aquatic exposure would be from this degradate. This degradate was also detected in livestock tissues and is included in the tolerance expression and the HED risk assessment. Its toxicity level was determined by HED to be equivalent or less than that of the parent. As for exposure, in the absence of fate data, the solubility was assumed to be equivalent to those of the parent and all abiotic degradation (hydrolysis and photolysis) and anaerobic metabolism processes, non existing.

Currently, quizalofop-p-ethyl is applied as a ground spray, aerial, air blast and soil injection applications. Trade and other names of products containing quizalofop-p-ethyl include: (1) Assure II; (2) Matador; (3) Dupont Assure II ;(4) MON 78746.

Quizalofop-p-ethyl is registered for several food crops and it is used to control the growth of perennial and annual grasses, weeds and vines. During the period of 2000-2006, approximate annual usage for quizalofop-p-ethyl and quizalofop-ethyl was 89,500 pounds. The usage data for quizalofop-p-ethyl and quizalofop-ethyl does not distinguish between the two chemicals. Quizalofop-ethyl did not have an active product registration during the period of data collection. The greatest poundage of quizalofop is used on soybeans (SLUA from BEAD). Quizalofop accounts for 30% of mint treated, 10% of canola/rape seed with a maximum of 20% treated, followed by dry beans/peas and garlic averaging 10% of the crop treated (SLUA from BEAD). While these data provide some insight into the historic use of quizalofop-p-ethyl, herbicide use changes with the varying resistance of pest plants; predicting total use prospectively is difficult since it may be based on the susceptibility of a particular pest plants to a specific herbicide.

Terrestrial exposure is based on direct spray application on food items including short grass, seeds, and broadleaf plants and insects resulting from applications of quizalofop-p-ethyl at the maximum label rates. Exposure to aquatic organisms is the result of runoff and spray drift from labeled applications, and is functionally the amount of compound in the water that would directly contact organisms. The magnitude of exposure estimates is largely dependent on the biology of the receptor (*e.g.,* food consumption rate), the use patterns, and environmental fate and transport characteristics of the pesticide.

5. OVERVIEW OF PESTICIDE USAGE

Quizalofop-p-ethyl is a herbicide that is used to control weeds in Non-Food/Non-feed uses (alfalfa, beets, carrot (including tops), swiss chard, grasses grown for seed, cottonwood/poplar plantations, non-agricultural uncultivated areas/soils, onion, ornamental and or shade trees, radish spinach and for Food and Feed uses (agricultural fallow/idle land, barley, succulent and dried beans, chinese cabbage, canola, eucalyptus, rape, cotton, crambe, flax, garlic, lentils, mint, peppermint and spearmint, dried and succulent peas, pineapple, soybeans, sugarbeets including tops, sunflower, and wheat). Quizalofop-p-ethyl is formulated as a wettable powder, soluble concentrate and liquid, and can be applied as various spray treatments such as; ground, soil injection, aerial and air blast.

The currently approved quizalofop-p-ethyl application rates for agricultural uses range from 0.0650 lb ai/acre (cotton) to 0.2063 lb ai/acre (pineapple) for a single application (BEAD 2007) with a seasonal maximum label rate of 0.4125 lb ai/acre (pineapple). For non-agricultural uses the maximum rate per application is 0.2063 lb ai/acre (ornamental and/or shade trees) with a seasonal maximum label rate of 0.4125 lb ai/acre (ornamental and/or shade trees) (BEAD 2007).

6. ENVIRONMENTAL FATE SUMMARY

Quizalofop-p-ethyl has a relative low water solubility of 0.4 mg/L. In organic solvents

such as acetone, hexane, and ethanol, quizalofop-p-ethyl is very soluble. It has a vapor pressure of 3 x mm Hg (@ 20'~) and a calculated Henry's law constant of 3.7 x atm-m3/mole. The hydrolysis rate is pH variable; with the half-life of 600 days at pH 5, 30 days at pH 7, and 2 days at pH 9. Supplemental studies also show that quizalofop-p-ethyl is moderately mobile with K_{ad}s of 1.5-1.9 in sandy loam soil, and immobile in silt loam soil with K_{ad}s of 16-20. Existing data from the Environmental Fate and Effects Division (EFED) files show conflicting results between laboratory studies and field studies. The acceptable laboratory aerobic soil metabolism study shows that quizalofop-p-ethyl degrades microbially with a half-life of 1 day in sandy loam and silt loam soils. However, quizalofop-p-ethyl was persistent in the field with half-lives of 145 and 364 days for studies conducted in IL and CA, respectively. The inconsistency in results between the laboratory and the field studies may be due to differences of pHs and microbial populations in the soil media used, and differences between the purposes of each study.

The acceptable fish accumulation study indicated that quizalofop-p-ethyl did not bioaccumulate with 28-day values of 1X and 4X for exposure concentrations of 0.004 and 0.04 mg/L, respectively.

As for the acid degradate, in the absence of data, previous assessment assumes that it is stable to both biotic and abiotic degradation and it has equivalent solubility to the parent.

7. ECOLOGICAL EFFECTS SUMMARY

Table 2 provides taxonomic groups and test species used to indicate the potential for ecological effects in this screening-level risk assessment. Within each of these very broad taxonomic groups, an acute and/or chronic endpoint is selected from the available test data.

Table 2. Taxonomic Groups and Most Sensitive Test Species Evaluated for Ecological Effects of quizalofop-ethyl and quizalofop-p-ethyl*

Taxonomic group	Example(s) of representative species	Endpoint Used
Birds[a]	Bobwhite quail (*Colinus virginianus*) Mallard duck (*Anas platyrhynchos*)	Acute LD_{50} Acute LC_{50} Chronic, NOAEC*
Mammals	Laboratory rat (*Rattus norvegicus*)	Acute LD_{50} NOAEC
Terrestrial insects	Honeybees (*Apis mellifera*)	Acute Oral LD_{50} N/A Acute Contact LD_{50}
Freshwater fish[b]	Rainbow trout (*Oncorhynchus mykiss*) Bluegill sunfish (*Lepomis macrochirus*) Fathead minnow *(Pimephales promelas)*	Acute LC_{50} Acute LC_{50} Chronic NOAEC

Table 2. Taxonomic Groups and Most Sensitive Test Species Evaluated for Ecological Effects of quizalofop-ethyl and quizalofop-p-ethyl*

Taxonomic group	Example(s) of representative species	Endpoint Used
Freshwater invertebrates	Water flea (*Daphnia magna*)	Acute EC_{50} NOAEC N/A no study submitted. Estimated values will be used in future assessments.
Estuarine/marine fish	Sheepshead minnow (Cyprinodon variegatus)	Acute LC_{50}
Estuarine/marine invertebrates	Mysid shrimp (*Mysidopsis bahia*) Eastern oyster (*Crassostrea virginica*)	Acute EC_{50} NOAEC N/A no studies submitted
Terrestrial plants*	Monocots – N/A Dicots – N/A	Seedling Emergence Vegetative Vigor EC_{25} N/A unacceptable studies submitted.
Vascular aquatic plants*	Duckweed *(Lemna gibba)* Tier1	Acute EC_{50} NOAEC N/A in previous risk assessments. Future risk assessment will use highest concentration value as NOAEC.
Non-vascular aquatic plants*	Green algae (*Selanastrum capricornutum)* Tier I	Acute EC_{50} NOAEC or EC_{05} N/A Since a maximum growth inhibition observed was 19% from the tier I study a NOAEC value from a Tier II test would quantify risks. However, EFED will quantify risks to listed species through estimated values and analog data.

[a]Birds are used as surrogates for terrestrial phase amphibians and reptiles (US EPA, 2004).
[b]Freshwater fish are used as surrogates for aquatic phase amphibians (US EPA, 2004).
*Studies were conducted on quizalofop-p-ethyl only. Studies not identified by an asterisk were conducted on quizalofop-ethyl.

8. ECOSYSTEMS AT RISK

The ecosystems that could be potentially at risk due to agricultural use of quizalofop-p-ethyl include terrestrial and aquatic (lakes, ponds, streams) habitats in proximity to quizalofop-p-ethyl use areas. These habitats may be at risk from drift and/or runoff of quizalofop-p-ethyl from use areas. The estuarine/marine ecosystems are likely at less risk since they are typically further from agricultural areas and are characterized by large volumes of water. However, in some areas adjacent to estuarine/marine environments where agriculture dominates the landscape, risks to estuarine/marine ecosystems cannot be excluded.

Organisms of concern include birds, mammals, reptiles, fish, and terrestrial and aquatic invertebrates, plants, and amphibians. The assessment endpoints are intended to reflect population sustainability and community structure within ecosystems and hence relate back to ecosystems at risk. If risks are expected for given species/taxa based on the screening-level assessment, then risks might be expected to translate to higher levels of biological organization. Identifying specific ecosystems at risk in a screening-level assessment is beyond the scope of the effort.

8.1 Receptors

The aquatic receptors likely to be exposed to quizalofop-p-ethyl include fish, invertebrates, aquatic stages of amphibians and plants living in waterways adjacent to or downstream from treated areas.

Terrestrial receptors likely to be exposed to quizalofop-p-ethyl include birds, mammals, reptiles, and terrestrial stages of amphibians that may occur in treated fields and terrestrial plants adjacent to, or down slope from treated areas.

8.2. Assessment Endpoints

Assessment endpoints are defined as "explicit expressions of the actual environmental value that is to be protected." Operationally, the environmental value is represented by an ecological entity and associated attributes or characteristics. The assessment endpoints for this ecological risk assessment will be survival, growth, and reproduction of terrestrial and aquatic animals and plants. Specifically, this assessment will address birds, mammals, reptiles, amphibians, terrestrial and aquatic invertebrates, terrestrial and aquatic plants, and fish. These endpoints, in turn, are meant to reflect population sustainability and community diversity within ecosystems.

Assessment endpoints and toxicity data used to evaluate the assessment endpoints are identified in **Table 2** and **Table 3**.

9. CONCEPTUAL MODEL

The conceptual model used to depict the potential ecological risk associated with quizalofop-p-ethyl is generic and assumes that as an herbicide, quizalofop-p-ethyl can affect terrestrial and aquatic organisms if environmental concentrations are sufficiently elevated as a result of the proposed label uses. A diagram of the conceptual model is presented in **Figure 1**. All of the use scenarios for quizalofop-p-ethyl involve spray applications such as: ground, aerial, air blast of the pesticide to foliage as well as soil injection. Although not evident from the diagram, quizalofop-p-ethyl degradation prior to runoff is explicitly considered. Runoff includes transport of quizalofop-p-ethyl and its degradate in a dissolved state as well as quizalofop-p-ethyl and its degradate adsorbed to eroded sediment.

As there are multiple spray applications of the pesticide to foliage of the proposed labeled use patterns, degradation on the foliage between applications is considered in the terrestrial assessments. A default foliar dissipation rate of 35 days will be used in the terrestrial risk assessments since no foliar dissipation studies are available. The default value represents an upper bound on expected foliar dissipation rates across all pesticides, based on data in Willis and McDowell (1987). For aquatic assessments, the microbial degradation on foliage is assumed stable, but wash-off of the foliage will be considered using the default wash-off coefficient assumption of 0.5 cm^{-1}. Spray drift will be considered in the aquatic assessments as a route of loading to the pond, with higher levels of spray drift for aerial applications than ground spray applications.

For terrestrial assessments, spray drift is not directly considered. However, since the evaluation of risk is done for on-field foliage, non-target foliage receiving spray drift should reduce pesticide loading and the assessment based on the on-field residues which would represent an upper bound estimate. A variety of food types (e.g., short grass, long grass, broadleaf plants) will be assessed regardless of the type represented by the target crop, as a variety of food types exist on and off the treated field.

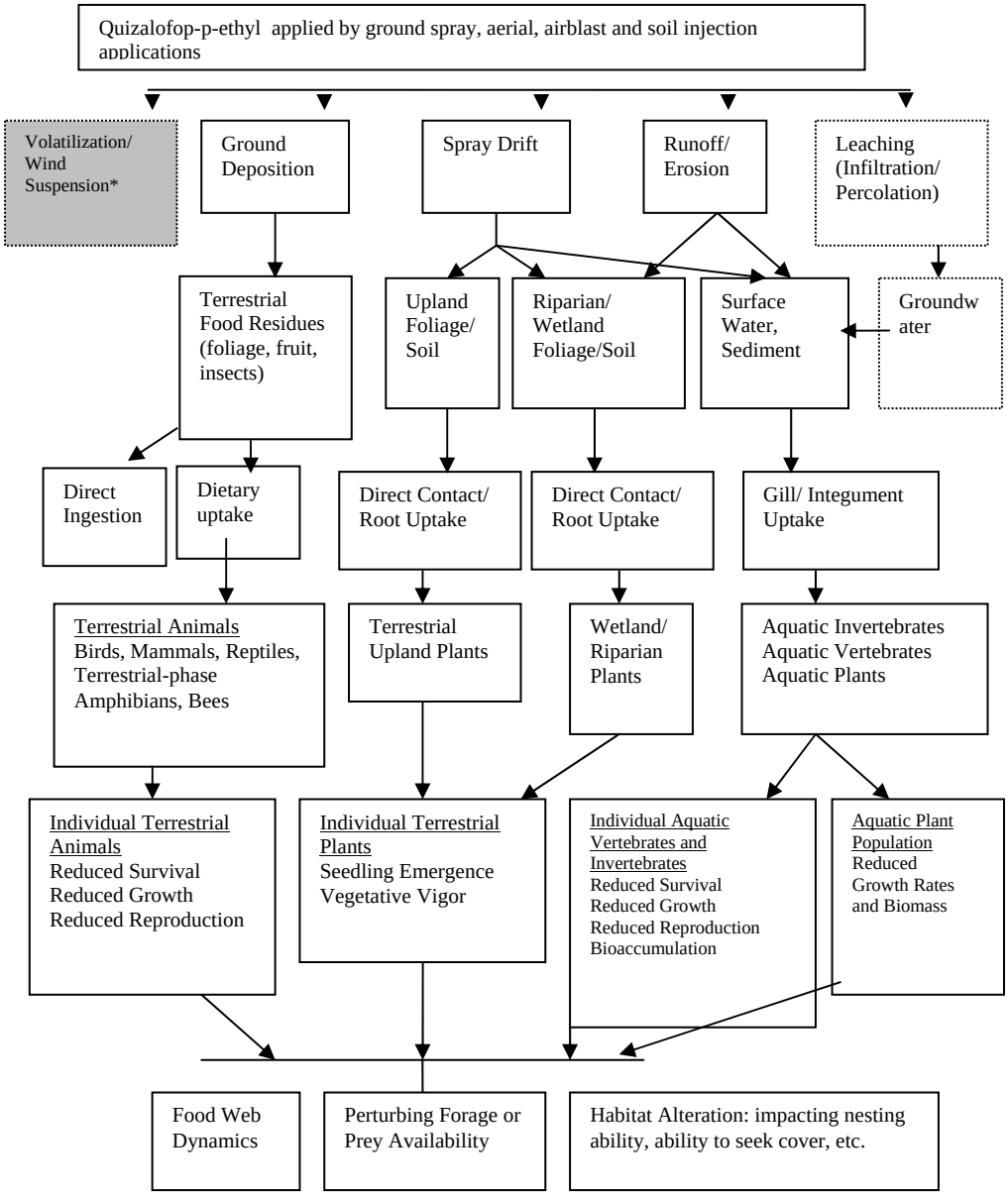
In aquatic environment, once quizalofop-p-ethyl reaches a water body, the pesticide is partitioned between the water column, suspended sediment, and bed sediment at a ratio based on the pesticides' physical/chemical properties. Degradation by abiotic hydrolysis, photolysis, and microbial mediated metabolism are taken into account. The route of exposure to fish is uptake of quizalofop-p-ethyl and its degradate dissolved in the water column through the gills and integument.

Quizalofop-p-ethyl does not bio-accumulate in fish. BCFs have 28-day values of 1X and 4X for exposure concentrations of 0.004 and 0.04 ml/L, respectively.

For birds and mammals, only the dietary route of exposure is considered. Uncertainties may include the lack of information on exposure from soil ingestion as well as exposure from other pathways such as inhalation and dermal routes.

Figure 1. Conceptual model of the fate/transport and effects of quizalofop-p-ethyl in the environment.

This updated conceptual model will be used in the next assessment which will incorporate additional applications



***** Volatilzation is not expected to be an exposure of concern due to a low vapor pressure of 3.0×10^{-7} mmHg@20^{o}C

10. RISK HYPOTHESES

Hypothesis: Nontarget terrestrial and aquatic animals and plants are at risk of direct and indirect effects resulting from labeled uses of quizalofop-p-ethyl.

11. ANALYSIS PLAN

The analysis plan is the final step in problem formulation. During this step measures of exposure and measures of effect are used to evaluate the risk hypotheses and are listed in **Tables 2 and 3** for a specific assessment endpoint. The RQ is obtained by dividing the measures of exposure for a particular assessment endpoint by the measures of effect for that endpoint.

11.1. Measures of Exposure

Measures of exposure for quizalofop-p-ethyl that will be used in this assessment are obtained from modeling efforts only, since national-scale monitoring data were not identified. Exposure models used for this assessment include the suite of standard exposure models commonly used in pesticide risk assessments (EPA, 2004). Generally, aquatic exposure estimates are generated from EFED models and incorporate maximum proposed use rates and empirically-derived fate properties. Aquatic exposure will be estimated using the PRZM/EXAMS model and will consist of aquatic EECs derived using a water body that is vulnerable and representative of static ponds and first order waterways.

Measures of exposure for terrestrial mammals, birds, reptiles, and amphibians similarly incorporate maximum proposed use rates but rely less on fate properties. Instead, terrestrial exposure estimates are derived directly from empirically determined observations of pesticide residues on various terrestrial food items. For numerous applications for a given use, the exposure model incorporates a first-order decay rate dependent on the soil half-life of the chemical. In place of unavailable foliar dissipation data, the default foliar dissipation half-life of 35 days will be used. The currently used terrestrial exposure model is TREX v.1.3.1.

Exposure to terrestrial plants will be estimated using the TerrPlant model that assumes quizalofop-p-ethyl drifts or moves with runoff to adjacent areas. However, acceptable terrestrial plant toxicity data has not been submitted. Therefore, risks to terrestrial plants can not be determined.

Based on preliminary EECs and the assumptions discussed above, chronic risks at the highest labeled application rate are expected for all non-listed and listed mammals and estuarine marine aquatic invertebrates (0.4125 lbs a.i./A per season). Risks are expected as well for non-listed and listed species of terrestrial plants inhabiting semi-aquatic and dry areas based on exposures of quizalofop originating from the maximum application rate. Because of the potential risk from direct effects to the listed and non-listed taxa described above, should exposure occur, listed species in all taxa may potentially be affected indirectly due to alterations in their habitat (*e.g.*, food sources, shelter, and areas to reproduce).

If the planned ecological risk assessment continues to indicate that quizalofop may potentially impact, either directly or indirectly, listed species or critical habitat, and therefore does not support a "not likely to adversely affect" determination, further refinements will be made. This will involve determining whether use of quizalofop "may affect" a particular listed species, and if so, whether it is "likely to adversely affect" the species, or in the case of designated critical habitat, whether use of the pesticide may destroy or adversely modify any principle constituent elements for the critical habitat, and if so, whether the expected impacts are "likely to adversely affect" the critical habitat. The first step in the process is to improve the exposure estimates based on refining the geographic proximity of quizalofop use and the listed species and/or critical habitat. If there is no geographic proximity, this information would support a determination that quizalofop use will have no effect on the species or critical habitat. If after conducting the first step of this analysis the Agency determines that geographic proximity exists, both potential direct effects and any potential indirect effects of the pesticide use will be examined. This process is consistent with the Agency's Overview Document. The Agency will consult as necessary with the U.S. Fish and Wildlife Service and National Marine Fisheries Service (collectively 'the Services'), consistent with the Services' regulations.

If the screening level risk assessment identifies potential concerns for indirect effects on listed species, the next step for EPA and the Services would be to identify which listed species and critical habitat are potentially implicated. Analytically, the identification of such species and critical habitat can occur in either of two ways. First, the agencies could determine whether the action area overlaps critical habitat or the occupied range of any listed species. If so, EPA would examine whether quizalofop potential impacts on non-endangered species would affect the listed species indirectly or directly affect a constituent element of the critical habitat. Alternatively, the agencies could determine which listed species depend on biological resources, or have constituent elements that fall into, the taxa that may be directly or indirectly impacted by quizalofop. Then EPA would determine whether the use of quizalofop overlaps the critical habitat or the occupied range of those listed species.

11.2. Measures of Effect

Aquatic plants and animals

(1) Freshwater Fish

Four acute toxicity studies using both the bluegill sunfish (Lepomis macrochirus) and rainbow trout (Oncorhynchus mykiss) indicated that quizalofop-ethyl is slightly to very highly toxic to freshwater fish on an acute toxicity basis based on values of LC_{50} 460 ppb (MRID 00146951), LC_{50} 870 ppb (MRID 00146680), LC_{50} 10720 ppb (MRID 00128210), LC_{50} 2820 ppb (MRID 00128210), . The bluegill sunfish was the most sensitive species tested with an LC_{50} value of 460 ppb (MRID 00128210). EFED used the LC_{50} value of 460 ppb for evaluating acute risks to freshwater fish. The guideline requirement for 72-1c and 72-1a acute aquatic fish was fulfilled (MRID 00146951).

A freshwater fish early life-stage chronic toxicity test on fathead minnow (Pimephales promales)

was used to evaluate the chronic toxicity of quizalofop-ethyl. Results from the study indicated a No Observed Adverse Effect Level (NOAEL) of 11 ppb based on decrease in larval survival, weight. EFED used this value for evaluating chronic risk to freshwater fish. This guideline requirement for 72-4a for the early life-stage fish was classified as supplemental (MRID150109).

(2) Freshwater Invertebrates

Three acute freshwater toxicity tests using the *Daphnia magna* indicated that quizalofop-ethyl is moderately toxic to freshwater invertebrates on an acute toxicity basis based on the EC_{50} values of 2120 ppb (MRID 00128210), 6400 ppb (MRID 00146951) and 3900 ppb (MRID 411616-01). EFED used the EC_{50} of 3900 ppb to evaluate risks to freshwater invertebrates which was not the most sensitive value. Therefore, the EC_{50} of 2120 ppb value will be assessed to use in future risk assessments. Although, the guideline requirement for 72-2a was fulfilled for the acute freshwater invertebrate study based on the EC_{50} of 3900 ppb, the EC_{50} of 2120 ppb value will be assessed to use in future use in risk assessments(MRID 411616-01) (MRID 00128210).

A freshwater invertebrate early life-stage toxicity test for freshwater invertebrates exposed to quizalofop-ethyl was not submitted to the Agency. No early life-stage invertebrate studies were submitted for freshwater invertebrates. Estimated values from ACRs will be accepted pending submission of requested a chronic estuarine marine invertebrate (mysid) study conducted on quizalofop-p-ethyl.

(3) Estuarine/Marine Fish

One estuarine/marine fish acute toxicity test, using the sheepshead minnow (Cyprinodon variegates), test indicated that quizalofop-ethyl is moderately toxic to estuarine/marine fish on an acute toxicity basis based on the LC_{50} value of 1400 ppb. Therefore, EFED used the LC_{50} value of 1400 ppb for evaluating acute risks to estuarine marine fish. The guideline requirement 72-3a for the acute toxicity to estuarine marine fish was fulfilled. (MRID 402422-09).

No early life-stage estuarine marine fish studies were submitted to the Agency. Estimated values from ACRs will be used in future risk assessments from acute and chronic freshwater fish and acute estuarine marine fish toxicity studies.

(4) Estuarine/Marine Invertebrates

Two estuarine/marine acute toxicity tests exposing the mysid shrimp, *Americamysis bahia*, to quizalofop-ethyl indicated that quizalofop-ethyl is highly toxic to estuarine/marine invertebrates on an acute toxicity basis based on the EC_{50} values of 250 ppb (MRID 402422-05) and 150 ppb (MRID 402422-04). EFED used the EC_{50} of 250 ppb to evaluate risks to estuarine marine invertebrates which was not the most sensitive value. Therefore, the EC_{50} 150 ppb value will be assessed to use in future risk assessments. Although, the guideline requirement for 72-2a was fulfilled for the acute estuarine marine invertebrate study based on the EC_{50} of 250 ppb, the EC_{50}

of 150 ppb value will be assessed to use in future use in risk assessments (MRID 402422-05) (MRID 402422-04).

No early life-stage estuarine marine invertebrate studies were submitted to the Agency. Since no chronic studies were submitted for either freshwater or estuarine marine aquatic invertebrates and exceedences may occur for higher use rates (pineapple and ornamental turf) especially for estuarine marine invertebrates, EFED requests an early life-stage estuarine marine invertebrate (mysid) study conducted on quizalofop-p-ethyl. to quantify risks for estuarine marine invertebrates. In addition, the NOAEC values from this estuarine marine invertebrate study will also be used to estimate NOAEC values for freshwater invertebrates derived from ACRs.

(5) Estuarine/Marine Mollusks

An estuarine/marine acute shell deposition toxicity test exposing the eastern oyster to quizalofop-ethyl indicated that quizalofop-ethyl is highly toxic to estuarine/marine mollusks on an acute toxicity basis based on the EC_{50} value of 187 ppb (MRID 402422-07). An Eastern oyster-larvae (bivalve) study was sited in earlier assessments as EC_{50} 79 ppb on canola (March 1997) and mint (February 1993) however no references were made.

(6) Aquatic Plants

The tier I test with non-vascular green alga *Selenastrum capricornutum* exposed to quizalofop-p-ethyl showed a maximum of 19 % inhibition at the mean measured test concentration of 1770 ppb (MRID 432356-01). Since an EC50 was not determined from any of the tier I aquatic plant tests, the value of EC50 > 1770 ppb will be used in future risk assessments to determine risks to aquatic non-vascular plants exposed to quizalofop-p-ethyl.

Two additional Tier I aquatic non-vascular plant studies using the freshwater diatom *Navicula pelliculosa* and the estuarine/marine diatom *Skeletonema costatum*, showed a maximum of 3% inhibition at a test concentration of 98 ppb and 1.8% stimulation at a test concentration of 82 ppb exposed to quizalofop-p-ethyl, respectively (MRID 432709-01 and MRID 432709-02). The aquatic vascular plant *Lemna gibba* from a Tier I study, showed no adverse response to quizalofop-p-ethyl exposure with EC50 >82.8 ppb (MRID 432585-01).

The results of the *Anabaena flos-aque* aquatic plant study (MRID 432356-02) conducted on quizalofop-p-ethyl was not incorporated in the 2005 risk assessment but will be in future risk assessments.

Non vascular plant NOAEC values were not determined for quizalofop-p-ethyl. In the absence of those data, EFED based its risk estimation for non vascular plants on data from the NOAEC for analog fenoxaprop-p-ethyl (27 ppb). It is understood that fenoxaprop-p-ethyl is more toxic ethyl to non vascular plants than quizalofop-p-ethyl (EC50 of 1770 ppb for quizalofop-p-ethyl vs 430 ppb for fenoxaprop -p-ethyl for Selanastrum capriconutum, the most sensitive species tested for

both chemicals), therefore using data from fenoxaprop-p-ethyl may overestimate risk for quizalofop-p-ethyl.

No effects occurred at the highest concentration of 82.8 ppb for *lemna gibba*, therefore EFED will use the NOAEC value of 82.8 ppb for vascular plants in future risk assessments.

Terrestrial organisms

(1) Birds

Five studies on the acute toxicity of quizalofop-ethyl (oral and dietary toxicity) to birds indicated that quizalofop-ethyl is practically non-toxic to the mallard duck (water-fowl) and the bobwhite quail (upland game bird) on acute oral and dietary toxicity basis. The LD_{50} values for the avian acute oral toxicity tests were: Mallard duck LD_{50} >2,000 mg kg-bw and Bobwhite Quail LD_{50}>2,000 mg /kg-bw. The LC_{50} values for the avian acute dietary toxicity tests were as follows: Mallard Duck LC_{50}>5,000 mg kg-diet; Bobwhite quail LC50 >5,000 mg /kg-diet; and Bobwhite quail LC50 >5620 mg/kg-diet. Therefore, EFED used the LD_{50} >2,000 mg kg-bw and LC_{50} >5,000 mg kg-diet values for evaluating acute oral and dietary risks to birds. NOAEC values were not determined. The guideline requirements 71-1 and 71-2 for the acute oral and dietary toxicity to birds were fulfilled. (MRID 00128210, MRID 00147574).

Based on provisional review of two avian chronic reproductive toxicity studies using quizalofop-p-ethyl, it appears that quizalofop-p-ethyl does not pose potential reproductive inhibition to birds based on a chronic toxicity basis. No reproductive effects were observed in a bobwhite quail study, resulting in a NOAEC value of 1000 ppm (MRID 466071-01).
However, there did appear to be a reduction in hatchability at the highest dose tested (1000 ppm a.i.) in the mallard duck study. There was an apparent reduction in hatchlings as a percentage of live 3-week embryos in the 1000 ppm a.i. treatment group, resulting in a NOAEC of 500 ppm (MRID 466071-02). However, it is not clear before a full review of the data whether this observed effect was statistically significant ($p>0.05$).

(2) Mammals

Wild mammal testing is required on a case-by-case basis only, and is dependent on the results of lower tier laboratory mammalian studies, intended use patterns, and pertinent environmental fate characteristics. In most cases, rat or mouse toxicity values obtained from the Agency's Health Effects Division (HED) are used as surrogates for wild mammal toxicity testing.
The acute toxicity of quizalofop-ethyl was evaluated using the laboratory rat. The acute toxicity of quizalofop-ethyl differed between male and female rats with females showing greater sensitivity than males. The LD_{50} values were 870 mg/kg bw (fema1es) and 1088 mg/kg bw(males) and a combined LD_{50} value of 979 m a g for both males and females. For the purposes of this risk assessment, the lower male-specific value of 870 mg/kg was used.

As with the mammalian acute toxicity data, the mammalian chronic toxicity data are obtained from the Agency's Health Effects Division (HED) and are considered representative of wild mammals. These studies provide adequate toxicity data on the potential effects of chronic quizalofop-p-ethyl exposure in mammals. In rats, the No Observable Adverse Effect Level (NOAEL) was 5mgkg/day for a decreased in male and female pup body weight, which corresponds to approximately to a dietary level of 100 ppm (mg a.i.kg feed). It should also be noted that the male adults and some male pups experienced testicular atrophy. In females signs of uterus atrophy were noticeable in the adults and the offspring.
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(3) Terrestrial Invertebrates

Acute toxicity of quizalofop-ethyl to terrestrial non-targeted beneficial insects was assessed where honey bees, Apis millifera, were exposed to quizalofop-ethyl via acute contact route. The acute contact LD_{50} value was 50ug/bee which classifies quizalofop-ethyl as practically non-toxic to non-targeted beneficial terrestrial insects on an acute contact toxicity basis. The study was classified as acceptable (MRID 150942).

(4) Terrestrial Plants

At this time EFED is requesting that the registrant re-submit terrestrial plant toxicity tests (e.g., Seedling Emergence and Vegetative Vigor Tests) with the typical-end-use product of quizalofop-p-ethyl. Previously submitted terrestrial plant studies were deemed unacceptable by EFED biological reviewers.

The measures of effects will either be the results of actual tests or will be derived or assumed based on other data. Where data is lacking and extrapolated effects endpoints cannot be reliably estimated, risk will be presumed unless data is submitted. In cases where risk is presumed, but cannot be quantified based on lack of data, conservative assumptions will be made, and some analyses will not be able to be conducted.

Assessment endpoints and toxicity data used to evaluate the assessment endpoints are identified in **Table 3** and **Table 4**.

Table 3. Summary of terrestrial assessment endpoints and proposed measures of effects for the screening level risk assessment of quizalofop-ethyl and quizalofop-p-ethyl. All studies are conducted on quizalofop-ethyl unless otherwise indicated

Assessment Endpoint	Measurement Endpoint
Avian Survival	Northern bobwhite quail Colinus virginianus LD_{50} > 2000mg/kg bw Mallard duck Anas platyrhynchos LD_{50} > 2000 mg/kg BW
Avian Reproduction and/or Survival***	Northern bobwhite quail (Colinus virginianus) NOAEC 1000 mg/kg diet Mallard duck (Anas platyrhynchos) NOAEC 500 mg/kg diet
Mammalian Survival	Laboratory rat Rattus rattus 870 mg/kg-bw
Mammalian Reproduction and/or Survival	Laboratory rat Rattus rattus NOAEC 100 mg/kg/diet NOAEL 5 mg/kg/day
Terrestrial Plants Survival and Growth***	Seedling emergence and vegetative vigor submitted studies were classified as unacceptable based on errors in toxicity determination and plant testing based on technical grade active ingredient (TGAI) instead of typical end use (TEP). These studies were conducted on quizalofop-p-ethyl. No quizalofop-ethyl seedling emergence and vegetative vigor studies were submitted.
Non-target Beneficial Insect Survival	Honey bee (acute contact) Apis meliferus 50 µg a.i./L

Table 4. Summary of aquatic assessment endpoints and proposed measures of effects for the screening level risk assessment of quizalofop-ethyl and quizalofop-p-ethyl. All studies are conducted on quizalofop-ethyl unless otherwise indicated

Assessment Endpoint	Measurement Endpoint
Freshwater Fish Survival	Rainbow trout (Oncorhynchus mykiss) LC_{50} 870 ppb Bluegill sunfish (Lepomis macrochirus) LC_{50} 460 ppb
Freshwater Fish Reproduction an/or Survival	Rainbow trout (Oncorhynchus mykiss) NOAEC 11 ppb
Freshwater Invertebrate Survival	Water flea (Daphnia magna) EC_{50} 3900*
Freshwater Invertebrate Reproduction and/or Survival	NOAECs will be estimated in future assessments based on ACRs, pending submission of a chronic estuarine marine invertebrate (mysid) toxicity study conducted on quizalofop-p-ethyl.
Marine/Estuarine Fish Survival	Sheepshead minnow (Cyprinodon variegatus) EC_{50} 1400 ppb
Marine/Estuarine Fish Reproduction and/or Survival	Chronic NOAEC 33ppb**
Marine/Estuarine Invertebrate Survival	Eastern oyster Crassostrea virginica EC_{50} 187 ppb Mysid shrimp Americamysis bahia EC_{50} 250 ppb*
Marine/Estuarine Invertebrate Reproduction and/or Survival	Request submission of a chronic estuarine marine invertebrate (mysid) toxicity study conducted on quizalofop-p-ethyl.
Aquatic Vascular and Non-vascular Plant Survival and Growth***	Tier I aquatic vascular plant (*Lemna gibba*) EC50>82.8 ppb Tier I aquatic vascular plant (*Lemna gibba*) NOAEC 82.8 ppb will be used in future risk assessments Tier I non-vascular plant *(Selanastrum capricornutum)* EC50>1770 ppb

* The most sensitive EC_{50} values for endpoints were not used to calculate RQs and will be reviewed for future risk assessments. Mysid shrimp, EC_{50} 150 ppb and acute freshwater invertebrate EC_{50} 2120 ppb

**** (2005 risk assessment calculated incorrectly as 513.3)

*** Studies conducted on quizalofop-p-ethyl

11.3. Preliminary Identification of Data Gaps for Fate and Ecological Assessment

Table 5 below, identifies fate and ecological studies, which are missing or are not acceptable, and may be requested to assess risk to the environment:

Table 5. Preliminary Identification of Data Gaps for Fate and Ecological Assessment*

Fate and Ecological Taxa studies	Description of study	Projected status of data gap	Basis for decision
Estuarine/marine fish	Chronic study for estuarine/marine fish was not submitted	Study not requested	Acute to chronic ratios will be sufficient to not request study
Chronic freshwater and estuarine marine invertebrate studies	Chronic toxicity data to freshwater and estuarine marine invertebrate studies were not submitted	Study requested for chronic estuarine marine invertebrate (mysid) conducted on quizalofop-p-ethyl. No study is requested for chronic freshwater invertebrate	Since no chronic invertebrate studies were submitted and chronic invertebrate exceedences may occur with estuarine marine invertebrates at higher application rates (pineapple and ornamental turf), a chronic estuarine marine invertebrate study is requested. ACRs will be sufficient to evaluate chronic freshwater invertebrates from receipt of the chronic estuarine marine invertebrate study.
Seedling Emergence and Vegetative Vigor Terrestrial Plant studies	Studies submitted for terrestrial plants based on quizalofop-p-ethyl were determined unacceptable due errors in toxicity determination and the use of TGAI instead of TEP formulation.	Additional studies requested	Seedling Emergence and Vegetative Vigor Terrestrial Plant studies conducted on quizalofop-p-ethyl are necessary to determine risks to terrestrial plants and buffers from spray drift.
Existing fate and eco-toxicity data on the degradate (quizalofop acid) to determine risks to aquatic organisms	Existing fate studies and ecotoxicity data were not submitted on the degradate (quizalofop acid)	Existing fate and eco-toxicty data from the registrant are not requested for the degradate at this time.	The parent quizalofop-p-ethyl can be easily converted to quizalofop acid. Additional ecotoxicity data such as; sediment toxicity studies are not requested for the degradate at this time unless additional fate and ecotoxicity data indicate an increased toxicity exposure to aquatic organisms.

Non-vascular plant study *(Selanastrum capricornutum)*	Maximum growth inhibition observed was 19% from a tier I study and a NOAEC could not be determined	Additional study not requested	Since a maximum growth inhibition observed was 19% from a tier I study and a NOAEC a Tier II test would quanitify risks. However, EFED will quantify risks to listed species through estimated values and analog data.
Foliar dissipation residue data	Foliar dissipation data studies or related data were not available	Study not requested	Chronic mammal exceedences will still occur with current NOAEC 100 mg/kg diet endpoint even if the halflife is 1 day. Therefore,A default foliar dissipation rate of 35 days will be used in the modeling in place of the data if study is not submitted.

*The fate and transport database for quizalofop-p-ethyl is complete.

12. OPEN LITERATURE

Previous assessments did not include open literature data as identified by ORD, MED ECOTOX literature search program.

13. NEW ASSESSMENT DECISION

EFED needs additional data (or will apply alternate effects assumptions) and would need to conduct new assessments for all registered outdoor uses. The new assessments are needed because of the following:

(a) Not all toxicity data were available for the 2005 assessment.
These data include: chronic study in estuarine/marine fish (72-4c), chronic life cycle toxicity studies in invertebrates (72-4b, 72-4d), seedling emergence and vegetative vigor for terrestrial plants (122-1/123-1) and aquatic toxicity data for the quizolofop acid degradate.

(b) Currently used models were not included in all risk assessments.

(c) Aquatic assessments were performed on “old” scenarios and models. New assessments are required to accurately assess toxic effects to aquatic.

(d) Some uses and application type scenarios were not assessed for ecological risk or did not include current terrestrial or aquatic models.
These scenarios include Non-Food/Non-feed uses (alfalfa, beets, carrot (including tops), swiss chard, grasses grown for seed, cottonwood/poplar plantations, non-agricultural uncultivated areas/soils, onion, ornamental trees, shade trees, radish, spinach and for Food and Feed uses (agricultural fallow/idleland, succulent and dried beans, snap beans,

chinese cabbage, canola, eucalyptus, rape, cotton, crambe, garlic, lentils, mint, peppermint and spearmint, dried and succulent peas, pineapple, soybeans, sugarbeets including tops.

(e) Open literature data, as identified by ORD, MED ECOTOX literature search program, were not included in previous assessments.

(f) A Tier II drinking water assessment of surface water was performed based on Index Reservoir settings (October 28, 2005, Section 3 New use registration request for quizalofop-p-ethyl (TARGA ^{TM}) on sunflowers, flax, wheat and barley (DP 310868) with the highest seasonal application rates of 0.1925 and 0.20625 lb ai/A. The simulation produced estimated drinking water concentrations (EDWC) of 5.25 ppb for acute exposure, 1.99 ppb for chronic exposure, and 1.34 ppb for cancer exposure. For ground water sources, the Tier I drinking water predicted EDWC of 0.15 ppb for both acute and chronic exposure. For this drinking water exposure purpose, the assessment is focused on the specific label uses.
All crop uses for quizalofop-p-ethyl according to the TARGA label are tabulated below based on 2005 drinking water exposure assessment.

Use	Modeling Scenario	Seasonal Rate	Application Scheme
Mint	OR	0.20625 (lb/ac)	2 applications
Dry Beans	MI	0.1925	2 applications
Sugarbeets	MN	0.171875	2 applications
Flax		0.165	2 applications
Canola and Crambe	ND	0.12375	2 applications
Cotton	CA, MS, NC	0.12375	2 applications
Soybeans	MS	0.12375	2 applications
Sunflowers		0.12375	2 applications
Lentils		0.09625	2 applications
Dry and Succlent Peas		0.09625	2 applications
Snap Beans	OR	0.09625	2 applications
Barleys		0.0825	1 application
Wheat	ND	0.0825	1 application

If additional crop uses have higher seasonal application rates, a new drinking water assessment needs to be completed.

14. SUMMARY OF RISK

Summary of Risks Identified for Use on Sunflowers, Flax, Wheat and Barley (DP 310868)

Estimated LOC exceedences for are summarized in **Table 6** below. The risk conclusions are based on previously conducted risk assessments and anticipated exceedences for maximum use rates. The most recent risk assessment conducted on sunflowers, flax, wheat and barley (D310868, 2005) employed the more current models used in the ecological risk assessment. The

label maximum single application rates for sunflowers, flax, wheat and barley are as follows: (1) sunflowers with a maximum seasonal rate of 0.12 lb ai /acre; (2) flax with a maximum seasonal rate of 0.165 lb ai /acre; and (3) wheat and barley with a maximum seasonal rate of 0.08 lb ai acre.

The maximum use and application rate for quizalofop-p-ethyl is for pineapples, ornamental and/ or shade trees at 0.4125 lb ai/A (2 applications@ 0.2063 lb ai/A and 7 day intervals). The 7 day interval was applied because label information did not specify intervals between applications. Anticipated LOC exceedences from the above maximum use rate would be chronic mammal with RQs ranging from 1.72 to 8.18. Terrestrial plants can not be assessed due to lack of acceptable data, however exceedences are anticipated for all modeled scenarios due to the chemical properties and mode of action of quizalofop-p-ethyl.

Aquatic EECs for the maximum application rates for labeled crops and PRZM/EXAMS scenarios need to be determined. However, chronic risks to estuarine marine invertebrates for quizalofop-p-ethyl are uncertain based on estimated values derived from the acute and chronic freshwater fish (rainbow trout). The RQ of 0.64 for chronic estuarine invertebrates derived from the estimated values for the 0.165 lb ai/A application scenario is close in value to the chronic LOC = 1.0 Table 7). Therefore, exceedences are anticipated for chronic risk to estuarine marine invertebrates with higher application rates. Since no chronic studies were submitted for chronic risks to either freshwater or estuarine marine invertebrates and uncertainty exists for possible LOC exceedences for chronic risks to estuarine marine invertebrates for higher application rate scenarios, a chronic study for estuarine marine invertebrate (mysid) study is requested.

Table 6. LOC exceedences for quizalofop-p-ethyl from use on sunflowers, flax, wheat and barley.*

Use	*Endpoint*	*Birds*	*Mammals*	*Terr. Plants*	*Insects*	*FW fish*	*SW Fish*	*FW Inverts*	*SW Inverts*	*Aquatic Plants*
sunflowers, flax, wheat and barley	*Acute*			*Not assessed*						
	Reproductive		✓							
pineapple, ornamental and/ or shade trees	*Acute*			✓						
	Reproductive		✓						✓	

- *All risk conclusions are based on previously conducted risk assessments (D310868) Degradate toxicity was not included*

✓ *Risk is anticipated to be > any of the Agency's LOC*

Blank cells indicate no LOC exceedences

Aquatic Organisms

Based on the Tier II (PRZM/EXAMS) modeling, the 2005 risk assessment on flax, sunflowers, barley and wheat showed no acute LOC exceedence for aquatic organisms. The highest modeled application rate scenario for the above crops was flax, which was based on 1 aerial application at a single rate of 0.165 lb ai/acre. **Table 7** summarizes the quizalofop-p-ethyl EECs (2.57 µg a.i./L (peak), 2.33 µg a.i./L (21-day), 2.03 µg a.i./L (60-day)) and the toxicity data used in the assessment on flax.

Endpoint selection for mysid shrimp and daphnia magna will be reviewed since the most sensitive endpoints were not selected for RQ calculation from the 2005 assessment. For acute toxicity to mysid shrimp the most sensitive endpoint EC_{50} 150 ppb and for *Daphnia magna* the most sensitive endpoint was EC_{50} 2120 ppb. The NOAEC for estuarine marine fish was calculated incorrectly as 513.3 ppb and would have to be determined based on the most sensitive endpoint selected. NOAECs were not determined for the Tier I vascular and non-vascular plants to address listed species concerns. Since no effects occurred at the single dose concentration value of 82.8 ppb for *Lemna gibba*, this value will be used as the NOAEC for vascular plants in future risk assessments. Although a 19% inhibition occurred based *Selanstrum capricornutum* (Tier I study), an additional study to determine a NOAEC value will not be requested at this time for non-vascular plants because estimated EECs would result in RQs which are below the LOC based on analog data. Many DERS are based on 1985-1988 statistical programs and outdated criteria, therefore these DERs will be reviewed and updated to current EPA standards. An Eastern oyster-larvae (bivalve) study was sited in earlier assessments as EC_{50} 79 ppb (on Canola March 1997 and Mint February 1993).

Table 7. Aquatic EECs and RQs for quizalofop-p-ethyl based on a single application of 0.165 lb ai/acre per season (the max.(EECs) label application rate to flax).

Taxa	Toxicity	EEC*	RQ
FW Fish	Acute LC50: 460 ppb	2.57 ppb (peak EEC)	RQ<LOC=(<0.01)
	Chronic NOAEC: 11 ppb	2.03 ppb (60-day EEC)	RQ<LOC=(<0.01)
FW Invertebrate	Acute EC_{50}: 3900 ppb***	2.57 ppb	RQ<LOC=(<0.01)
	Chronic NOAEC ++ Estimated NOAEC value of 26.8 based on an acute EC50 value of 2120 ppb would result in RQ< LOC=0.09****	2.57 ppb	N/A
FW Vascular Aquatic Plants	Acute EC_{50}: >82.8 ppb	2.57 ppb	RQ<LOC=(<0.02)
	NOAEC: was not determined (*Lemna gibba)* tier 1stud y . However, the NOAEC value of 82.8 ppb will be used in future risk assessments	2.57 ppb	N/A
Non-vascular Plants and Algae	Acute EC_{50}: (>1770ppb *Selenastrum capricornutum*)	2.57 ppb	RQ<LOC=(<0.01)
	NOAEC:not determined	2.57 ppb	N/A
Estuarine/Marine Fish	Acute LC_{50} 1400 ppb *(Sheepshead minnow)*	2.57 ppb	RQ<LOC=(<0.01)
	Chronic NOAEC 33ppb** (2005 risk assessment calculated incorrectly as 513.3)	2.03 ppb	RQ<LOC=(<0.06)
Estuarine/Marine Invertebrates	Mysid shrimp, EC_{50}: 250 ppb***	2.57 ppb	RQ<LOC=(<0.01)
	Chronic NOAEC: ++ Estimated NOAEC value of 3.6 based on an acute EC50 value of 150 ppb would result in RQ< LOC=0.64****	2.33 ppb (21-day EEC)	N/A
Estuarine/Marine Mollusc	Acute EC_{50}: 187 ppb	2.57 ppb	RQ<LOC=(<0.01)

*Derived for one application of 0.165lb a.i./acre aerial application (flax)
** Chronic NOAEC derived using acute to chronic ratio due to lack of submitted data.
*** The most sensitive EC_{50} values for endpoints were not used to calculate RQs and will be reviewed for future risk assessments. Mysid shrimp, EC_{50} 150 ppb and acute freshwater invertebrate EC_{50} 2120 ppb
**** Estimated values were derived from quizalofop-ethyl acute and chronic freshwater fish (rainbow trout) studies
++ Data not available

There are insufficient data to establish a definitive toxicity endpoint for estuarine marine and freshwater invertebrate chronic effects for quizalofop-ethyl. To estimate potential chronic estuarine marine and freshwater invertebrate endpoints for quizalofop-ethyl the relationship between established acute and chronic freshwater fish (rainbow trout) endpoints for quizalofop-ethyl were considered. A ratio was determined between the acute and chronic freshwater fish

endpoints used for RQ calculation from quizalofop (870 ppb acute freshwater fish (rainbow trout)/ 11 ppb chronic freshwater fish (rainbow trout) =79). The largest ratio between acute endpoint and chronic endpoint was applied to the most sensitive quizalofop acute estuarine marine and freshwater invertebrate value to derive estimated chronic endpoints as described in **Table 8.**

Table 8 Summary of Calculations for Estimated Endpoints

ENDPOINT DESIRED For Quizalofop-p-ethyl	Acute/Chronic Quizalofop-ethyl =ratio	Acute Endpoint quizalofop/ratio= endpoint	Estimated Endpoint
Chronic freshwater invertebrate daphnia(endpoint in section 3)*	870 ppb/11 ppb=79 rainbow trout	2120 ppb/79=26.8 ppb	NOAEC 26.8 ppb
Chronic estuarine marine invertebrate mysid(endpoint in section 3**)	870 ppb/11 ppb=79 rainbow trout	150 ppb/79=1.8 ppb	NOAEC 1.8 ppb

*Chronic freshwater invertebrate daphnia: 2.57 ppb/NOAEC 26.8 ppb= RQ 0.09 for 0.165 lb ai/acre
**Chronic estuarine marine invertebrate mysid: 2.57ppb/NOAEC 1.8 ppb= RQ 1.4 for 0.165 lb ai/ acre

Terrestrial Organisms

No acute or chronic exceedences occurred for birds from the 2005 assessment for sunflowers, flax, barley and wheat. Also, no acute or chronic exceedences will occur for birds based on the proposed highest maximum seasonal rate of 0.4125 lb a.i./A (2 applications @ 0.2063 lb ai/A and 7 day intervals) and the non-definitive LD_{50} bw (>2000 ppm) and LC_{50} (>5000 ppm) diet. Acute RQs were not calculated for birds from uses on sunflowers, flax, barley and wheat.. However, because the LD_{50} bw (>2000 ppm) and LC_{50} (>5000 ppm) diet were greater than the highest dosage administered for bobwhite quail, quizalofop was characterized as practically non-toxic to birds.

Based on provisional review of two avian chronic reproductive toxicity studies using quizalofop-p-ethyl, it appears that quizalofop-p-ethyl does not pose potential reproductive inhibition to birds based on a chronic toxicity basis.
Chronic RQs ranged from <0.01- 0.08 from the NOAEC 500 mg/kg-diet value and <0.01-0.04 NOAEC 1000 mg/kg-diet value from uses on sunflowers, flax, barley and wheat.

Table 9. Avian dietary based chronic RQ values based on a bobwhite quail NOAEC=1000 and a mallard duck NOAEC= 500 mg/kg for 0.12, 0.17 and 0.08lb ai/A application scenarios derived from the 2005 risk assessment.

Table 9. Avian dietary-based chronic RQ values for proposed uses of Quizalofop-p-ethyl based on upper-bound Kenaga residues. (Bobwhite Quail NOAEC=1000; and Mallard duck NOAEC= 500 mg/kg)

Use/App. Method	Application Rate lbs. ai/A (# app / interval, days)	Food Items	Upper Bound EEC (mg/kg)[a]	Chronic RQ (EEC/ NOAEC)
Sunflower	0.12/ 1 application	Short grass	28.80	0.06[1] 0.03[2]
		Tall grass	13.20	0.03[1] 0.01[2]
		Broadleaf plants/small insects	16.20	0.03[1] 0.02[2]
		Fruits, pods, seeds, and large insects	1.80	<<0.01[1] <<0.01[2]
Flax	0.17/ 1 application	Short grass	40.80	0.08[1] 0.04[2]
		Tall grass	18.70	0.04[1] 0.02[2]
		Broadleaf plants/small insects	22.95	0.05[1] 0.02[2]
		Fruits, pods, seeds, and large insects	2.55	0.01[1] <0.01[2]
Barley/Wheat	0.08/ 1 application	Short grass	19.20	0.04[1] 0.02[2]
		Tall grass	8.80	0.02[1] 0.01[2]
		Broadleaf plants/small insects	10.80	0.02[1] <0.01[2]
		Fruits, pods, seeds, and large insects	1.20	<0.01[1] <0.01[2]

1. The mallard duck NOAEC of 500 mg/kg/diet was used in estimating chronic RQs

2. The bobwhite quail NOAEC of 1000 mg/kg/diet was used in estimating chronic RQs

No acute LOC exceedences occurred for 15g, 35g and 1000g mammals that consume short grass, tall grass, broadleaf plants/small insects, fruits pods large insects and seeds for all modeled scenarios (2005 assessment) **Table 10.** No acute LOC exceedences will occur for mammals based on the proposed highest maximum seasonal rate of 0.4125 lb ai/A (2 applications@ 0.2063

lb ai/A and 7 day intervals).

Chronic LOCs were exceeded for 15 g and 35 g mammals that consume short grass, tall grass, broadleaf plants/small insects and 1000 g mammals that consume short grass with chronic RQs ranging from 0.01 to 3.54 for upper-bound Kenaga residues (2005 assessment **Table 11).** The chronic RQs were also exceeded for the mean Kenaga values as shown in (2005 assessment) **Table 12**. It is therefore expected that higher application rate use scenarios will result in even greater chronic RQs exceedences for mammalian organisms.

Therefore, chronic exceedences (dose based) will occur for mammals based on the proposed highest maximum seasonal rate of 0.4125 lb ai/A (2 applications@ 0.2063 lb ai/A and 7 day intervals) with RQs ranging from 0.05 to 8.8.

Table 10. Mammalian dose-based acute RQ values for proposed uses of Quizalofop-ethyl based on a rat LD_{50} = 870 mg/kg-bw and upper-bound Kenaga values.

Use/App. Method	Application Rate lbs. a.i./A (# app / interval, days)	Body Weight, g	Mammalian Acute Risk Quotients (upper-bound Kenaga residues)				
			Short Grass	Tall Grass	Broadleaf Plants/Small Insects	Fruits/pods/ large insects	Seeds
Sunflower	0.12/ 1 application	15	0.01	0.01	0.01	<0.01	<0.01
		35	0.01	0.01	0.01	<0.01	<0.01
		1000	0.01	<0.01	<0.01	<0.01	<0.01
Flax	0.17/ 1 application	15	0.02	0.01	0.01	<0.01	<0.01
		35	0.02	0.01	0.01	<0.01	<0.01
		1000	0.01	<<0.01	0.01	<0.01	<0.01
Barley and Wheat	0.08/ 1 application	15	0.01	<0.01	0.01	<0.01	<0.01
		35	0.01	<0.01	<0.01	<0.01	<0.01
		1000	<<0.01	<0.01	<0.01	<0.01	<0.01

Table 11. Mammalian dose-based chronic RQ values for proposed uses of Quizalofop-p-ethyl based on a rat reproductive NOAEL of 5 mg/kg /day and upper-bound Kenaga residues.

Use/App. Method	Application Rate lbs. a.i./A (# app / interval, days)	Body Weight, g	Mammalian Chronic Risk Quotients (upper-bound Kenega values)				
			Short Grass	Tall Grass	Broadleaf Plants/Small Insects	Fruits/pods/ large insects	Seeds
Sunflower	0.12/ 1 application	15	**2.50***	**1.15***	**1.41***	0.16	0.03
		35	**2.13***	0.98	**1.20***	0.13	0.04
		1000	**1.14***	0.52	0.64	0.07	0.02
Flax	0.17/ 1 application	15	**3.54***	**1.62***	**1.99***	0.22	0.05
		35	**3.02***	**1.39***	**1.70***	0.19	0.02
		1000	**1.62***	0.74	0.91	0.10	0.02
Barley and Wheat	0.08/ 1 application	15	**1.67***	0.76	0.94	0.10	0.02
		35	**1.42***	0.65	0.80	0.09	0.023
		1000	0.76	0.35	0.43	0.05	0.01

*****exceeds the chronic risk LOC (RQ $\geq$ 1.0) for non-listed and listed species.

Table 12. Mammalian dose-based chronic RQ values for proposed uses of Quizalofop-p-ethyl based on a rat reproductive NOAEL of 5 mg/kg /day and mean Kenaga residues.

Use/App. Method	Application Rate lbs. a.i./A (# app / interval, days)	Body Weight, g	Mammalian Chronic Risk Quotients (Mean Kenega values)				
			Short Grass	Tall Grass	Broadleaf Plants/Small Insects	Fruits/pods/ large insects	Seeds
Sunflower	0.12	15	0.9	0.40	0.50	0.07	0.02
		35	0.80	0.30	0.40	0.06	0.01
		1000	0.40	0.20	0.21	0.03	0.01
Flax	0.17	15	**1.30***	0.53	0.66	0.09	0.05
		35	**1.07***	0.50	0.60	0.19	0.02
		1000	0.60	0.24	0.30	0.05	0.01
Barley and Wheat	0.08/ 1 application	15	0.60	0.30	0.31	0.05	0.01
		35	0.50	0.21	0.30	0.04	0.01
		1000	0.30	0.11	0.14	0.02	<<0.01

*****exceeds the chronic risk LOC (RQ $\geq$ 1.0) for non-listed and listed species.

Seedling emergence and vegetative vigor studies were classified as unacceptable, therefore RQs were not calculated for terrestrial plants.

15. RESIDUES OF QUIZALOFOP-P-ETHYL AND QUIZALOFOP ACID DEGRADATE IN WATER AND THE TERRESTRIAL ENVIRONMENT

The acceptable aerobic soil metabolism study shows that quizalofop-p-ethyl degrades microbially with a half-life of 1 day in sandy loam and silt loam soils. Degradation products are quizalofop acid, phenolic compounds, and CO_2. Supplemental studies also show that quizalofop-p-ethyl is moderately mobile with K_{ads} of 1.5-1.9 in sandy loam soil, and immobile in silt loam soil with K_{ads} of 16-20.

Existing data from the Environmental Fate and Effects Division (EFED) files show conflicting results between laboratory studies and field studies. The acceptable laboratory aerobic soil metabolism study shows that quizalofop-p-ethyl degrades microbially with a half-life of 1 day in sandy loam and silt loam soils. However, quizalofop-p-ethyl was persistent in the field with half-lives of 145 and 364 days for studies conducted in IL and CA, respectively. The laboratory studies indicate that dissipation occurs quickly via aerobic and anaerobic degradation, however, the field studies suggest that quizalofop-p-ethyl is persistent in the field. The differences may be due to differences of the microbial populations in the different soil media.

DRINKING WATER RESIDUE PROFILE

The Agency does not have monitoring data available to perform a quantitative drinking water risk assessment for quizalofop-P ethyl at this time. A Tier II drinking water assessment prepared by the Environmental Effects and Fate Division (EFED) is summarized below (D310868, J. Lin, 10/25/2005).

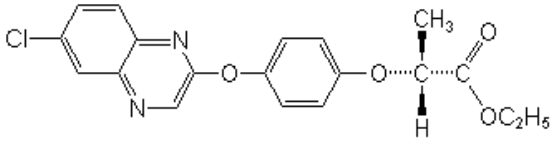
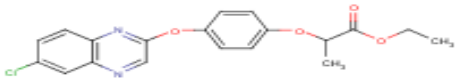
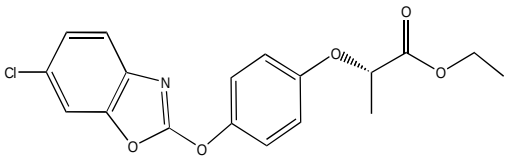
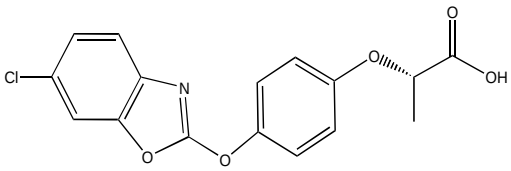
Quizalofop ethyl is rapidly converted to quizalofop acid, which appears to be persistent. Likely residues of quizalofop ethyl and the quizalofop acid in surface drinking water were estimated using the PRZM -EXAMS to simulate pesticide transport as a result of runoff and erosion from agricultural fields. For evaluating ground water residues, a Tier I Screening Concentration In Ground Water (SCIGROW) model was used. Among the various uses, a scenario on dry beans at 0.1925 lb ai/A/season in the state of Michigan was used to predict the "worst case" estimate of drinking water concentration (EDWCs). The EDWCs obtained by these two models are summarized in **Table 13.**

Table 13. Drinking Water EDWCs for Quizalofop ethyl (ppb)

Model Used	Acute	Chronic	Cancer
PRZM/EXAMS	5.25	1.99	1.34
SCIGROW	0.15	0.15	

New drinking and ground water assessments will be required due to proposed maximum seasonal application rates resulting in 0.4125 lb ai/A for ornamental trees, shade trees and pineapple. Chemical structures for quizalofop and fenoxaprop analogs are summarized in **Table14**.

Table 14. Chemical name and structure of quizalofop-p-ethyl and quizalofop-ethyl
Chemical structure of quizalofop acid, the degradate of concern, is not available.
Chemical name and structure of fenoxaprop -p-ethyl and fenoxaprop-ethyl
(analogs used to derive estimated toxicity values for non-vascular plants)

Common Name/Number	Chemical Structure
Quizalofop-p-ethyl	
Quizalofop-ethyl	
Fenoxaprop-p-ethyl	
Fenoxaprop-p	

The following test materials are listed as quizalofop-ethyl:

INY 6202
NC 302
Lot 8002
INY 6202-15
NB 9083-86

The following test materials are listed as quizalofop-p-ethyl:
IN 79376
DPX 79376

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

November 7, 2007

This memorandum supersedes the memorandum of the same subject dated 9/17/07; DP#'s 343684 and 342231

SUBJECT: **Quizalofop-ethyl** (PC 128711) and **Quizalofop-p-ethyl** (PC 128709) Health Effects Division (HED) Problem Formulation for Registration Review. **DP# 342230.**

FROM: Catherine Eiden, Chief
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Office of Pesticide Programs

TO: Russell Wasem, CRM
Reregistration Branch
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Office of Pesticide Programs

Executive Summary. Quizalofop-ethyl was first registered in 1988 and quizalofop-p-ethyl (the R-enantiomer) was first registered in 1990. As a result neither chemical was subject to review under the reregistration process recently completed under the Federal Insecticide Fungicide and Rodenticide Act (FIFRA) and the Food Quality Protection Act (FQPA) as of August 3, 2006 for chemicals registered prior to 1984. Consequently, neither a Reregistration Eligibility Decision (RED) nor a Tolerance Reregistration Eligibility Decision (TRED) was issued.

The most recent HED human health risk assessments were completed in August of 2006. They reflect current registrations and uses of quizalofop-ethyl and quizalofop-p-ethyl. The toxicity and exposure databases are adequate to support these human health risk assessments and make safety findings under FQPA. Liver effects and decreases in body weight gain and food consumption as a result of repeat dosing were seen in subchronic and chronic/carcinogenicity studies in rats, mice, and dogs. The risk assessments reflect current FQPA policies, address susceptibility of infants and children, the FQPA Safety Factor, and aggregate exposures. The current risk estimates are below Agency levels of concern for all population subgroups as a result of dietary exposures (inclusive of food

mice, and dogs. The risk assessments reflect current FQPA policies, address susceptibility of infants and children, the FQPA Safety Factor, and aggregate exposures. The current risk estimates are below Agency levels of concern for all population subgroups as a result of dietary exposures (inclusive of food and drinking water). These risk estimates are generally conservative and health-protective and should not underestimate exposure and risk. Residential exposures to quizalofop-ethyl and quizalofop-p-ethyl are not anticipated; there are no registered residential uses. Based on the combination of low hazard (via dermal and inhalation routes) and exposure potentials, HED determined that occupational risk assessments were not required. No new data are required**.** HED anticipates no revisions to the risk assessments for existing uses of quizalofop-ethyl and quizalofop-p-ethyl.

Introduction. Quizalofop-ethyl (including its R-enantiomer, quizalofop-p-ethyl) is a systemic herbicide that is rapidly absorbed by treated foliage and translocated to the roots and other growing points of the plant. Affected plant tissues become necrotic/chlorotic and die leaving treated plants stunted and non-competitive. It controls annual and perennial grasses. It can be applied using ground boom equipment and by fixed wing aircraft as broadcast and banded applications. It has low application rates.

Products containing quizalofop-ethyl and quizalofop-p-ethyl are currently registered. Quizalofop-ethyl is a 50/50 racemic mixture of R- and S-enantiomers. Quizalofop-p-ethyl is the purified R-enantiomer. The pesticidally active isomer is the R-enantiomer (quizalofop-p-ethyl). HED determined that the toxicological profile of the 50/50 racemic mixture (quizalofop-ethyl) and the R-enantiomer (quizalofop-p-ethyl) are similar, and that the currently available toxicity data on quizalofop-ethyl are adequate to support risk assessments reflecting uses of both quizalofop-ethyl and quizalofop-p-ethyl.

Use Pattern and Exposure Potential. It is registered for use on a variety of food/feed use agricultural crops and non-agricultural crops. Food uses include: grains, legumes, cotton, garlic, mint, sugar beets, sunflower, pineapple, and Chinese cabbage. Several crops are grown for seed only, including: carrot, alfalfa, beets, Swiss chard, radish, onion, and spinach. Non-agricultural crops include: cottonwood and poplar plantations and uncultivated areas, such as fencerows and roadsides. No lawn, sidewalk, driveway, tennis court, or similar public areas have been registered as use sites. Based on its registered use patterns, there is the potential for dietary (via food and water) and occupational exposures to quizalofop-ethyl and quizalofop-p-ethyl. Homeowner exposures via residential uses are not expected.

Hazard Characterization. Quizalofop-ethyl and quizalofop-p-ethyl are considered to be toxicologically similar. HED based this determination on a comparison of toxicity data submitted for the registration of quizalofop-ethyl and a subset of toxicity data for quizalofop-p-ethyl. Specifically, toxicity data available for quizalofop-p-ethyl included: an acute oral study in the rat, 90-day subchronic feeding studies in the rat and mouse, and three mutagenicity studies. Results from these studies were similar to results obtained from the same studies using

quizalofop-ethyl. Conclusions regarding the toxicity of quizalofop-ethyl are applicable to quizalofop-p-ethyl.

The toxicity database for quizalofop-ethyl was reviewed in 1994 and reevaluated in October 1997 to specifically assess sensitivity in infants and children under FQPA. The toxicity database was found to be substantially complete and adequate to assess risk under FQPA. HED has determined that the currently available toxicity data on quizalofop-ethyl are adequate to support risk assessments reflecting uses of both quizalofop-ethyl and quizalofop-p-ethyl. No additional toxicity data for either quizalofop-ethyl or quizalofop-p-ethyl are required. No toxicity studies involving human subjects were relied upon in any of the risk assessments conducted for quizalofop-ethyl or quizalofop-p-ethyl.

Toxicity endpoints selected for risk assessment in 1994 were confirmed in the 1997 reevaluation. The FQPA Safety Factor was reduced to 1X and the current risk assessments reflect this reduction. HED believes the FQPA Safety Factor reflected in the current risk assessment for quizalofop-ethyl is supported by the available toxicity and exposure information on quizalofop-ethyl and that the risk assessments are protective of human health.

The toxicity database includes acceptable developmental studies in rats and rabbits, reproduction/fertility studies in rats, subchronic studies in rats and dogs, chronic studies in rats and dogs, carcinogenic studies in rats and mice, mutagenicity screens, and a 28-day dermal toxicity study in rats, as well as information on the metabolism and pharmacokinetics of quizalofop-ethyl. A search of the open literature was conducted for toxicity studies involving quizalofop-ethyl using NIH's PubMed, SCRIUS, Science Direct, and a full text medical journals search. No *in vivo* toxicity testing studies or other information that would be relevant to HED's human health risk assessments were found from 1995 to the present. NCEA's IRIS shows no activity on quizalofop-ethyl since the late 1980s. No new toxicity data have been submitted.

The liver is the primary target organ for repeated doses of quizalofop-ethyl. Effects on the liver manifested as increased liver weights and histological changes in the liver. Liver effects and decreases in body weight gain and food consumption as a result of repeat dosing were seen in subchronic and chronic/carcinogenicity studies in rats, mice, and dogs. Metabolism and excretion occur quickly in the rat. No toxic effects attributable to a single oral dose of quizalofop-ethyl were identified.

It is classified in Toxicity Category III (low acute toxicity) for dermal, inhalation, eye and skin irritation. No localized or systemic effects were associated with a dermal dose of up to 2000 mg/kg/day. As a result of this finding and a lack of developmental effects, no dermal toxicity endpoint was selected. In addition to quizalofop-ethyl's classification as a Category IV inhalation toxicant, its use pattern indicates low single and seasonal maximum application rates, its vapor pressure is 1×10^{-4} kPa (meaning it is considered a non-volatile chemical for outdoor uses), and risk estimates (MOEs) for inhalation exposures are approximately 1000 or greater. As a result of these findings, no inhalation toxicity endpoint was selected. Based on the lack of dermal effects and negligible inhalation exposures, occupational risk assessments were neither required nor conducted.

Quizalofop-ethyl does not appear to be a neurotoxic chemical; there were no signs of neurotoxicity in the available toxicity studies for quizalofop-ethyl. Specifically, treatment-related effects on brain weight or histopathology (non-perfused) of the nervous system were not observed in any study, there was no evidence of developmental anomalies in the nervous system of the fetus at maternal doses up to 300 mg/kg/day in rats and 60 mg/kg/day in rabbits, and there was no evidence of neurotoxicity on the functional development of offspring during the postnatal portion of the developmental toxicity study in rats.

No special sensitivity was seen in rats and rabbits *in utero* as a result of exposure to quizalofop-ethyl. Exposure to quizalofop-ethyl at doses causing liver and body weight effects in adult animals did not lead to effects in fetuses. Exposure to quizalofop-ethyl at doses causing body weight effects in adult animals resulted in similar effects in offspring. As a result, the FQPA Safety Factor was reduced to 1X.

Califrornia lists quizalofop-ethyl as a reproductive toxicant. Quizalofop-ethyl was first listed in 1994 under California's Proposition 65: the Safe Drinking Water and Toxics Enforcement Act and the Toxics Release Inventory (TRI). The listing was based on a 26-week feeding study in dogs conducted in 1982 in which 2 of 6 male dogs showed atrophy of some seminiferous tubules at the highest dose tested (10 mg/kg/day). The effect was not so severe as to cause disturbance of spermatogenesis. These effects could not be repeated in a follow-up study conducted over a 52-week period in 1985 in which dogs were fed the same doses as in the 1982 study. There were no treatment-related effects in the follow-up study.

Quizalofop-ethyl is currently classified as a "Group D " carcinogen, i.e., not classifiable as to human carcinogenicity.

Given the toxicological and chemical similarities between quizalofop-ethyl and the R-enantiomer (quizalofop-p-ethyl), the two compounds will be referred to as quizalofop in the remainder of this document.

To assess risk associated with chronic dietary (oral) exposures to quizalofop, a chronic reference dose (cRfD) of 0.009 mg/kg/day has been established. The cRfD was selected from a combined chronic/carcinogenicity toxicity study in rats in which no effects were noted at 0.9 mg/kg/day and anemia and liver effects were noted at 4 mg/kg/day. The cRfD is based on the lowest and most conservative endpoint in the toxicity database. The cRfD reflects a 100-fold safety factor for inter- and intra-species variability. Because the FQPA safety factor was reduced to 1X, the chronic population adjusted dose (cPAD) is equivalent to the cRfD. The cRfD selected to assess risks from chronic dietary exposures to quizalofop is protective of the reproductive effects seen in 26-week study in the dog. Toxic endpoints for acute dietary and occupational risk assessments have not been selected for the reasons discussed above.

Dietary Exposure and Risk Estimates. Dietary risk estimates for exposures to quizalofop in food and drinking water are below levels of concern. They reflect current policy and practice. The tolerance expression and residues of concern for risk assessment for registered uses need not be revised. The dietary risk assessments include all permanent tolerances (Section 3 registrations). There are adequate residue data reflecting the use of all existing formulations on

representative commodities; the dietary exposure database is complete. No new residue data have been submitted. There are no issues concerning residue chemistry and no new data are required.

An acute dietary risk assessment was not conducted because no toxic endpoint attributable to a single oral dose was identified in the toxicity database. Chronic dietary risk for the general population was estimated to be 11% of the chronic Population Adjusted Dose (cPAD) and 29% of the cPAD for children 1 to 2 years old. Chronic dietary risk estimates are conservative and unrefined. They reflect tolerance level residues and 100% crop-treated values were assumed for all commodities. Drinking water exposures were assessed for a scenario for dry peas in Michigan using direct incorporation of estimated environmental concentrations (EECs) into the chronic dietary analyses. The drinking water assessment reflects current policy and practice. The current dietary risk assessments provide conservative, health protective, high-end estimates of exposure to quizalofop residues in food and water. The current dietary risk assessments are not expected to underestimate risks.

Residential Exposure and Risk Estimates. Quizalofop-containing products are not registered for use in/on residential or public recreational sites; there are no registered lawn or garden uses. No residential risk assessments were conducted.

Aggregate Risk Estimates. Risk estimates for aggregate exposures to quizalofop are below levels of concern. Average exposures in food and drinking water were combined and compared to the appropriate endpoint to estimate chronic aggregate risk.

Occupational Exposure and Risk Estimates. As stated previously, occupational risk assessments are not required and have not been conducted for quizalofop. Quizalofop is not toxic via the dermal route; therefore, no dermal endpoint was selected. Quizalofop is a Category III Inhalation Toxicant indicating low toxicity by the inhalation route, it is not volatile, and it has low use rates. All of these factors indicate that use of quizalofop will not lead to inhalation exposures of concern. To support this qualitative assessment, HED has estimated risks from inhalation exposures for workers applying and handling quizalofop products for a number of high acreage crops using a screening-level analysis. This screening-level analysis uses maximum use rates, maximum acreage, and the cRfD to estimate inhalation risks. Risk estimates based on inhalation exposures of pesticide handlers (mixers, loaders, applicators) for barley, flax, sunflower, wheat, cotton, pineapple, and non-crop areas are all below HED's level concern. The Margins of Exposure (MOEs) resulting from this screening assessment range from >500 to 160,000 are not of concern as they are well above 100. In summary, based on quizalofop's low toxicity via the dermal and inhalation routes, its physical/chemical properties, low exposure potential, and a screening-level analysis indicating that there are no inhalation exposures of concern, occupational risk assessments were not conducted. A 12-hour Restricted Reentry Interval (REI) has been established and is reflected on the labels of all registered products.

Public Health and Incident Reports. Very few incidents of poisoning associated with exposures to quizalofop have been reported. This finding supports HED's risk assessment, which indicates that both exposure to and toxicity of quizalofop are low. Since 1988 when it was first registered, a total of 18 reports of poisoning incidents have been reported. The Poison Control

Center (PCC), reporting from 1993 to 2005, cites 10 incidents. All individuals affected were adults; the effects reported were headache, eye and throat irritation. OPP's Incident Data System (IDS) reports 8 incidents. The incidents are associated with a variety of symptoms including rashes, cramping, swelling, diarrhea, nausea, dizziness, lethargy, and hypothermia. None of these effects is consistent with the toxicity database for quizalofop. Quizalofop is not an acutely toxic chemical, there is no indication of neurotoxicity, and the majority of toxic effects seen in the animal studies were systemic effects that were the result of repeated dosing, such as liver and body weight effects. The National Institutes of Occupational Safety and Health's Sentinel Event Notification System (NIOSH SENSOR) reported 5899 cases of poisoning incidents between 1998 and 2003. None of these reported incidents was associated with quizalofop.

Cumulative Risk Assessments. The Agency has not determined whether quizalofop shares a common mechanism of toxicity with other chemical substances, and whether a cumulative assessment is warranted. The following reference contains information regarding determination of common mechanisms of toxicity: "Guidance for Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity" (January 29, 1999). To date, the Agency has assessed the potential for a common mechanism of toxicity for four groups of chemicals: organophosphates, N-methyl carbamates, S-triazines, and chloroacetanilides. If quizalofop is determined to share a common mechanism of toxicity with other substances, then methods for aggregating exposures and risks will be developed. Until quizalofop is scheduled for a common mechanism determination and a decision is made, the Agency would not *a priori* assume a common mechanism of toxicity exists for quizalofop and other substances.

Data Requirements. No new data are required.

Tolerances and International Harmonization. Permanent and time-limited tolerances for quizalofop from the most recent CFR are provided in the table below along with international tolerances. The Codex Alimentarius Commission has not established Maximum Residue Limits (MRLs) for residues of quizalofop in/on various raw agricultural and processed commodities. Canada and Mexico have established MRLs for quizalofop. US tolerances and MRLs on raw agricultural commodities from these countries do not appear to have been harmonized. However, meat, milk, poultry and egg tolerances with the exception of milk, fat have been harmonized between Canada and the US. The residue definitions appear to be the same for raw agricultural commodities, but slightly different for animal commodities.

Quizalofop

US		Canada	Mexico	Codex
Residue Definition:				
Combined residues of the herbicide quizalofop (2-[4-(6-chloroquinoxalin-2-yl oxy)phenoxy]propanoic acid) and quizalofop ethyl (ethyl-2-[4-(6-chloroquinoxalin-2-yl oxy)phenoxy]propanoate), all expressed as quizalofop ethyl 40CFR.180.441		ethyl (RS) 2-[4-(6-chloroquinoxalin-2-yloxy) phenoxy] propionate, including the acid metabolites of (RS)2-[4-(6-chloroquinoxalin-2-yloxy) phenoxy] propanoic acid, all expressed as quizalofop-ethyl	quizalofop	none
Commodity Tolerance (ppm) /Maximum Residue Limit (mg/kg)				
Bean, dry	0.4	0.15 [1]		
Bean, succulent	0.25			
Beet, sugar, roots	0.1			
Beet, sugar, tops	0.5			
Cowpea, forage	3.0			
Cowpea, hay	3.0			
Pea, dry	0.25			
Pea, field, hay	3.0			
Pea, field, vines	3.0			
Pea, succulent	0.3	0.05 (dry or succulent not specified)		
Potato	-		0.3	
Soybean flour	0.5			
Soybean, hulls	0.02			
Soybean, meal	0.5			
Soybean, soapstock	1.0			
Soybean	0.05	0.05	0.05	
Residue Definition:				
Combined residues of the herbicide quizalofop (2-[4-(6-chloroquinoxalin-2-yl oxy)phenoxy]propanoic acid), quizalop-ethyl (ethyl-2-[4-(6-chloroquinoxalin-2-yl oxy)phenoxy]propanoate), and quizalofop-methyl (methyl 2-[4-(6-chloroquinoxalin-2-yl-oxy)phenoxy]propanoate, all expressed as quizalofop ethyl		As above	As above	none
Commodity Tolerance (ppm) /Maximum Residue Limit (mg/kg)	0.05	0.05		

US		Canada	Mexico	Codex
Cattle, meat	0.02	0.02		
Cattle, meat byproducts	0.05	0.05		
Egg	0.02	0.02		
Goat, fat	0.05	0.05		
Goat, meat	0.02	0.02		
Goat, meat byproducts	0.05	0.05		
Hog, fat	0.05	0.05		
Hog, meat	0.02	0.02		
Hog, meat byproducts	0.05	0.05		
Horse, fat	0.05	0.05		
Horse, meat	0.02	0.02		
Horse, meat byproducts	0.05	0.05		
Milk	0.01	0.01		
Milk, fat	0.25	0.05		
Poultry, fat	0.05	0.05		
Poultry, meat	0.02	0.02		
Poultry, meat byproducts	0.05	0.05		
Sheep, fat	0.05	0.05		
Sheep, meat	0.02	0.02		
Sheep, meat byproducts	0.05	0.05		
Residue Definition:				
Combined residues of the herbicide quizalofop-p ethyl ester [ethyl (*R*)-(2-[4-((6-chloroquinoxalin-2-yl)oxy)phenoxy)propanoate], and its acid metabolite quizalofop-p [*R* -(2-(4-((6-quinoxalin-2-yl)oxy)phenoxy)propanoic acid], and the *S* enantiomers of both the ester and the acid, all expressed as quizalofop-p-ethyl ester		As above	As above	none
Commodity Tolerance (ppm) /Maximum Residue Limit (mg/kg)				
Barley, grain	0.05			
Barley, hay	0.05			
Barley, straw	0.05			
Beet, sugar, molasses	0.2			
Canola, meal	1.5			
Canola, seed	1.0	0.05		
Cotton, undelinted seed	0.1		0.05	
Flax, seed	0.05	0.05		
Lentil, seed	0.05	0.05		
Peppermint, tops	2.0			
Spearmint, tops	2.0			
Sunflower, seed	1.9			
Wheat, forage	0.05			
Wheat, grain	0.05			
Wheat, hay	0.05			
Wheat, straw	0.05			

US		Canada	Mexico	Codex
Beet, sugar root (time limited 06/14/1999)	0.1	0.2 (top or bottom not specified)		
Beet, sugar, tops (time limited 06/14/1999)	0.5			
Vegetable, foliage of legume, except soybean, subgroup 7A (time limited 06/14/1999)	3.0			
Vegetable, legume, group 6 (time limited 06/14/1999)	0.25			
Pineapple (Regional registration)	0.1			

[1] Interim Marketing Authorization, including adzuki beans, dry beans, dry lima beans, kidney beans, mung beans, navy beans, and pinto beans.

Considerations

In preparation of this problem formulation document for quizalofop-ethyl in support of registration review the following has been considered:

- Search for and review of the most current human health risk assessments, including occupational/residential and dietary assessments conducted for new uses, Section 18 Emergency Exemptions, and Special Local Needs (24Cs) using internal Lotus Notes databases
- Review of the most recent decisions regarding hazard characterization, the adequacy and completeness of the toxicity database, the FQPA Safety Factor neurotoxicity, thyroid and immune system effects, and cancer issues to ensure their reflection in the most recent risk assessments
- Search of the OPPIN database to identify data submitted that have not been reviewed or included in the most current risk assessments
- Review E Jackets to clarify the status of a use
- Review of the most current labels to ensure all current registrations have been included in the most recent risk assessments
- Conduct a search of the general literature for information on quizalofop-ethyl not captured in current risk assessments
- Review of labeled uses and use information from BEAD
- Review of tolerances listed in Part 140 of the Code of Federal Regulations (CFR) Section 180.441
- Review of Codex Alimentarius and Canadian and Mexican MRLs to identify tolerance harmonization issues
- Determine if most recent risk assessments reflect current policies
- Review of poisoning incidents

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IV. Glossary of Terms and Abbreviations

ai	Active Ingredient
AR	Anticipated Residue
CFR	Code of Federal Regulations
cPAD	Chronic Population Adjusted Dose
CSF	Confidential Statement of Formula
CSFII	USDA Continuing Surveys for Food Intake by Individuals
DCI	Data Call-In
DEEM	Dietary Exposure Evaluation Model
DFR	Dislodgeable Foliar Residue
DNT	Developmental Neurotoxicity
DWLOC	Drinking Water Level of Comparison
EC	Emulsifiable Concentrate Formulation
EDWC	Estimated Drinking Water Concentration
EEC	Estimated Environmental Concentration
EPA	Environmental Protection Agency
EUP	End-Use Product
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FQPA	Food Quality Protection Act
FOB	Functional Observation Battery
GENEEC	Tier I Surface Water Computer Model
IR	Index Reservoir
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOC	Level of Concern
LOAEL	Lowest Observed Adverse Effect Level
µg/g	Micrograms Per Gram
µg/L	Micrograms Per Liter
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter
MOE	Margin of Exposure
MRID	Master Record Identification (number). EPA's system of recording and tracking submitted studies.
MUP	Manufacturing-Use Product
NA	Not Applicable
NAWQA	USGS National Ambient Water Quality Assessment
NPDES	National Pollutant Discharge Elimination System
NR	Not Required
NOAEL	No Observed Adverse Effect Level
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
PCA	Percent Crop Area
PDP	USDA Pesticide Data Program
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval

ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/EXAMS	Tier II Surface Water Computer Model
Q_1*	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
RAC	Raw Agriculture Commodity
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RQ	Risk Quotient
SCI-GROW	Tier I Ground Water Computer Model
SAP	Science Advisory Panel
SF	Safety Factor
SLN	Special Local Need (Registrations Under Section 24©) of FIFRA)
TGAI	Technical Grade Active Ingredient
USDA	United States Department of Agriculture
UF	Uncertainty Factor
WPS	Worker Protection Standard