US EPA ARCHIVE DOCUMENT

Triflumizole Summary Document: Registration Review

March 2007

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Triflumizole Summary Document
Registration Review Docket
March 2007

REGISTRATION REVIEW
Preliminary Work Plan
for
Triflumizole

CASE 7003

March 2007

Approved by: Debra Edwards

Debra Edwards, Ph. D.
Director
Special Review and Reregistration Division

Date: March 22, 2007

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I. Preliminary Work Plan

Introduction:

The Food Quality Protection Act (FQPA) of 1996 amended the Federal Fungicide Insecticide and Rodenticide Act (FIFRA) to mandate a new program: registration review. All pesticides distributed or sold in the United States generally must be registered by 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 product labeling. The new registration review program is intended to make sure that, as the ability to assess and reduce 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 to make sure that as change occurs, products in the marketplace can continue to be used safely. Information on this program is provided at: http://www.epa.gov/oppsrrd1/registration_review/.

The Agency has begun to implement the new registration review program, and plans to review each registered pesticide approximately 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 clearly what it knows about the pesticide and what additional risk analyses and data or information it believes are needed to make a registration review decision.

Anticipated Risk Assessment and Data Needs:

The Agency anticipates conducting a comprehensive ecological risk assessment, including an endangered species assessment for all triflumizole uses. One additional environmental fate study will be needed for this assessment. Further, EPA plans to revisit occupational risk assessments for grapes and pineapple seed pieces. Additional data to support the human health risk assessments are not needed.

Ecological Risk:

- Although two ecological risk assessments for triflumizole have been completed in 2001 and 2006, the Agency has neither conducted a comprehensive risk assessment nor a risk assessment which supports a complete endangered species determination. Please refer to Section III, Ecological Risk Assessment Problem Formulation, for a detailed discussion of the available environmental risk assessment and the additional risk assessment needs.

- The Agency anticipates needing a special study that is a combination of a Foliar Dislodgeable Residue Dissipation study (OPPTS Guideline no. 875.2100) and a Soil Residue Dissipation study (OPPTS Guideline no. 876.7200) in order to conduct a complete ecological risk assessment, including an endangered species assessment for all uses.

Human Health Risk:

For the currently registered uses of triflumizole, the Agency believes that previously completed dietary and residential assessments are adequate. However, the occupational risk assessment

needs updating using current database information. No additional test data or exposure information are needed, but the hazard characterization will be updated to reflect findings from recently reviewed toxicity studies. Please refer to Section IV of this document, Human Health Effects Scoping Document, for a detailed discussion of the available human health risk assessments.

Timeline:

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

Activities	Estimated Month/Year
Phase 1: Opening the docket	
Open Public Comment Period for Triflumizole Docket	March 2007
Close Public Comment Period (Mar 28 – June 25)	June 2007
Phase 2: Case Development	
Develop Final Work Plan (FWP)	Aug 2007
Issue DCI	May 2008
Data Submission (last date for)	May 2010
Open Public Comment Period for Preliminary Risk Assessments	Sept 2011
Close Public Comment Period	Nov 2011
Phase 3: Registration Review Decision	
Open Public Comment Period for Proposed Reg. Review Decision	February 2012
Close Public Comment Period	April 2012
Final Decision and Begin Post-Decision Follow-up	August 2012
Total (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 the triflumizole case.

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 levels (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.

Stakeholders are also specifically asked to provide information and data in the following areas:

1. confirmation on the following label information
    a. sites of application

b. formulations
c. application methods and equipment
d. maximum application rates
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 90th 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 90th 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

Triflumizole is not identified as causes 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. However, the Agency invites submission of other existing water quality data for this chemical. To the extent possible, data elements outlined in Appendix A of the "OPP Standard Operating Procedure: Inclusion of Water Quality & Impaired Water Body Data in OPP's Registration Review Risk Assessment & Management Process" should be provided in order to insure that they can be used quantitatively or qualitatively in pesticide risk assessments (see: http://www.epa.gov/oppsrrd1/registration_review/water_quality_sop.htm).

Next Steps:

After the comment period closes in late June of 2007, the Agency will issue a Final Work Plan for this pesticide.

II. FACT SHEET

Background Information:

- Triflumizole Registration Review case number: 7003
- Triflumizole PC Code: 1228879 / CAS#: 686994-11-1
- Technical registrant: Chemtura USA Corporation
- First approved for use in a registered product in 1989.
- There are eight FIFRA Section 3 active registrations for Triflumizole.
- Not subject to reregistration; thus, no Reregistration Eligibility Decision (RED) was prepared.
- Chemical Review Manager: Jacqueline Guerry (guerry.jacqueline@epa.gov)
- Product Manager: Mary Waller (waller.mary@epa.gov)
  Tamue Gibson (gibson.tamue@epa.gov)

Use and Related Information:

- Triflumizole is a broad spectrum foliar fungicide for controlling plant diseases by inhibiting ergosterol biosynthesis in fungi (destabilizes fungal cell walls).
- It is used to treat powdery mildew, leaf spot, scab, & various blights, rusts, and rots.
- Uses: almond, apple, cantaloupe, cherry, cucurbit vegetables, grape, filbert/hazelnut, honeydew, pear, pumpkin, squash, strawberry, and watermelon. Also used on ornamentals in greenhouses, shadehouses, nurseries (including Christmas tree/conifer plantations), and interiorscapes.
- Up to 80,000 lbs active ingredient (ai)/year is used on food crops (EPA estimates).
- Formulated as a wettable powder, soluble concentrate, and as a water dispersible granule; it is applied via airblast, ground boom, & high pressure hand-wand and certain aerial (fixed wing and rotary) equipment.
- Use information, such as application rates and number of applications, can be found in the support documents from the Biological and Economic Analysis Division in the docket.

Recent Regulatory Actions:

- A final rule for triflumizole was issued on 3/15/2006 (71 FR 13724) which established a tolerance on filberts.
- There are no pending IR-4 petitions for triflumizole.
- There are no Section 24(c) registrations for triflumizole.
- In 2004 and 2005, Texas requested and received emergency exemptions for use of triflumizole for use on broccoli, collards, dandelion, kale, and kohlrabi.
- In 2004 and 2005, Texas also requested and received crisis exemptions to treat cilantro, collards, dandelion, kale, kohlrabi, mustard greens, parsley, Swiss chard, and brassica leafy vegetables.
- Section 18 tolerances (70 FR 49354) were established on August 23, 2006 and will expire on December 31, 2009, for the following crops: broccoli, Chinese nappa cabbage,

collards, coriander leaves, dandelion leaves, kale, kohlrabi, mustard greens, parsley leaves, Swiss chard, and turnip greens.

Ecological and Environmental Fate Risk Assessment Status:

- The most recent environmental fate and ecological risk assessment was conducted on February 7, 2006.
- Based on all available data and the predicted exposures, triflumizole may pose an acute and chronic risk to mammals, and an acute risk to endangered freshwater fish.
- Additional assessment work is necessary due to the following factors:
  - Not all toxicity data were available for assessments conducted prior to 2006: These data include: acute toxicity studies in estuarine/marine fish (72-3a) and invertebrates (72-3b, 72-3c), chronic study in estuarine fish (72-4c), chronic life cycle toxicity studies in invertebrates (72-4b, 72-4d), and the toxicity studies in aquatic (122-2/123-2) and terrestrial plants (122-1/123-1),
  - Currently used models and triflumizole degradates were included in only one risk assessment (Section 3 registration for use on filberts),
  - Some uses and application type scenarios were not assessed for ecological risk. These scenarios include Christmas trees, conifer seed, grapes, pear, and pineapple seed,
  - Open literature data, as identified by ORD and the MED ECOTOX literature search program, were not included in previous assessments.

Human Health Risk Assessment Status:

- Based on recent assessments, there are no dietary or occupational risks that exceed the Agency's level of concern (LOC).
- The Agency anticipates some minor revisions to the triflumizole risk assessments.
  - The current hazard characterization does not adequately reflect available findings from reviewed neurotoxicity studies and their impact on the reserved developmental neurotoxicity study (DNT) requirement, or the current status of the 28-day inhalation study requirement, which has been waived. The hazard characterization will be updated to reflect these findings and decisions.
  - EPA will revisit the occupational risk assessments and determine whether revised worker risk assessments are needed for grapes and pineapple seed pieces.

Tolerances:

- There are 11 tolerances for food crops, 20 tolerances for meat, milk, fat, and meat by-products, and 10 (Section 18 Emergency Exemptions) time limited (until December 31, 2009) US tolerances listed under 40 CFR § 180.476 Triflumizole; tolerances for residues.
- Maximum Residue Levels (MRLs) for triflumizole have not been established by the Codex Commission. However, Japan, Australia, and the Netherlands have set MRLs.
- Please refer to Section IV of this document (pp. 45-47), Human Health Effects Scoping Document, for a listing of tolerance levels and MRLs.

Data Call-In Status:

- No Data Call-Ins have been issued for triflumizole.

Labels:

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

III. ECOLOGICAL RISK ASSESSMENT PROBLEM FORMULATION

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: March 22, 2007

MEMORANDUM

Subject: EFED Problem Formulation for Triflumizole Registration Review
PC Code: 128879
DP Barcode: 332490 and 332491

To: Michael Goodis, Risk Manager
Mark Howard, Risk Manager Reviewer
Registration Division (7505P)

From: Iwona L. Maher, Chemist, ERBI
Marie Janson, Environmental Scientist, ERBI 03/22/07
Thuy Nguyen, RAPL, ERBI
Nancy Andrews, Branch Chief, ERBI
Environmental Fate and Effects Division (7507P) 03/.29/07

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

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 triflumizole on apples, cherries, Christmas trees, conifer seed, filberts, cucurbits, grapes, ornamental woody and herbaceous plants (flowering or non- flowering), pear, pineapple and strawberries, 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:

- February 07, 2006 Section 3 assessment for newly proposed uses on Filberts (D312295)
- March 03, 2002 Tier I Estimated Drinking Water Assessment for Triflumizole including Degradates (D281356)
- May 21, 2001 Section 3 assessment for newly proposed uses on Cherries, Strawberries, Cucurbits, and Ornamentals (D242426).

Risks, as identified in these assessments, are:

1. For mammals: Chronic risk to mammals, based on a 1 lb a.i./A per season use (filbert) (RQ of 53 to 0.34). Acute and chronic risks exist for 2-3 lb a.i./A per season uses (grapes and cherries); the RQs ranged from 0.21 to <0.01 for acute risk and from 150 to 1 for chronic risk.
2. For freshwater fish: Endangered Species LOCs are exceeded on an acute basis. These exceedences, if re-evaluated using the current aquatic models, may be not be repeated.
3. For birds, since acute endpoints could not be established, triflumizole was characterized as practically non toxic to birds, and acute risk to birds was not assumed. However, if the non-definitive values of LD50 =2510 ppm and LC50 = 5620 ppm were used in the modeling, acute risk LOC exceedences exist for birds with cherries uses (RQ of 0.33 to <0.01). Analogs data or other data may be needed to better characterize the risks for birds.

No incidents of wildlife or aquatic species poisonings associated with uses of triflumizole were found in the Ecological Incident Information System (EIIS) database.

2. DATA GAPS AND ANTICIPATED DATA NEED

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

- *Chronic estuarine/marine fish study*: a registrant-submitted study was determined invalid due to the statistically-different values from solvent. For ecological modeling purposes, the acute to chronic ratios will be sufficient to not request new study.
  Decision: study not requested.

- *Marine diatom study*: a submitted study classified as supplemental because the initial cell density was greater than required. This taxon (marine diatom) represented the most sensitive species for non-vascular plants.
  Decision: study not requested.

- *Anaeorobic aquatic metabolism study*: study not submitted. Default value (stable) used in aquatic modeling did not trigger any LOC exceedence for aquatic organisms.
  Decision: study not requested.

- *Aeorobic aquatic metabolism study*: study not submitted. Default value (stable) used in aquatic modeling did not trigger any LOC exceedence for aquatic organisms.
  Decision: study not requested.

- *Foliar dissipation residue data* (from field residue trials conducted for triflumizole applications to variety of crops): not required, but if acceptable studies were available, they could potentially influence the modeling results since mammals exceeded Agency LOCs when a default half life value of 35 days were used in modeling. Triflumizole degrades with half-lives less than 10 days under hydrolysis and photolysis (water and soil), and 18 days in aerobic soil metabolism study. This indicates that foliar dissipation half-life may be shorter than 35 days. A screen using T-REX, which was based on cherries use (3 lb ai/A/season) and a default foliar dissipation rate of 35 days results in acute (endangered species and restricted use) risks to birds and mammals and chronic risk to mammals. However, if a half life of 3 days or shorter was assumed, only chronic risk (RQ < 5) to mammals will be anticipated.
  Decision: studies or data are requested to minimize uncertainties in modeling for mammal acute risk. Note that, based on the modeling results as presented above, the foliar dissipation half-life study will be of value only if the resulting half-life is 3 days or shorter.

3. PESTICIDE TYPE, CLASS, AND MODE OF ACTION

Triflumizole([1-[1-((4-chloro-2(trifluoromethyl) phenyl)imino)-2-propoxyethyl]-1H-Imidazole]; CAS 68694-11-1) is an imidazole that is effective in inhibiting ergosterol biosynthesis in fungi. Many fungi must synthesize ergosterol which is a compound needed for the stabilization of membranes that make up cell walls.

4. STRESSOR SOURCE AND DISTRIBUTION

The source of the stressor considered is triflumizole fungicide (PC Code 128897) and triflumizole degradates containing the 4-chloro-2-trifluoromethyl aniline moiety.

During the HED MARC meeting on February 26, 2002, the MARC committee has not excluded the possible toxicological concern for the metabolites containing the 4-chloro-2-trifluoromethyl aniline moiety. The half-lives for aerobic soil metabolism, hydrolysis and photolysis are calculated collectively for the parent and degradates of concern. The estimated concentrations represent the degradates containing the 4-chloro-2-trifluoromethyl aniline moiety namely, FD-1-1, FM-6-1, FA-1-1, FM-5-1, FM-3-1, FD-2-1, and FM-8-1 along with the parent compound for use in calculating the toxicity to aquatic species.

Triflumizole is not likely to be persistent under most environmental conditions and, except for soils in a sand textural class with low organic material, unlikely to be very mobile. Triflumizole degradates may be more persistent than the parent based on the longer half-lives for the combined residue. The half-lives derived for aquatic photolysis, soil photolysis and aerobic soil metabolism for total residues correspond to 12.7 days, 8 days and 44 days, respectively. The relatively high K_{OC} values in non-sand soils and the moderate adsorption characteristics in sandy soils with organic carbon content greater than one percent suggest that triflumizole has low potential to reach groundwater. The K_{OC} values for the degradate, FD-1-1 suggest that it is more mobile than the parent compound. Triflumizole will reach surface water in both the dissolved form and sorbed onto soils and organic material for several weeks following application.

Currently, triflumizole is applied via various spray treatments such as; ground spray , soil drench, aerial, microtube, high and low volume ground sprayers, hand held wand, dipper, chemigation, mist sprayer and sprinkler irrigation. The extent of acreage treated with triflumizole is unknown, but the crops to be treated are collectively grown throughout the United States.

Terrestrial exposure is based on direct spray application on food items including short grass, seeds, and broadleaf plants and insects resulting from applications of triflumizole 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

Triflumizole is a fungicide that is used as foliage, flower, nut spray, and soil drench to control of fungus and blights on apples, cherries, Christmas trees, conifer seed, filberts, cucurbits, grapes, ornamental woody and herbaceous plants (flowering or non- flowering), pear, pineapple and

strawberries. Triflumizole is formulated as a wettable powder, soluble concentrate and liquid, and can be applied as various spray treatments such as; ground, soil drench, aerial, microtube, high and low volume ground sprayers, hand held wand, dipper, mist sprayer, chemigation and sprinkler irrigation.

The currently approved triflumizole application rates for agricultural uses range from 0.5 lb ai/acre (apples and cherries) to 0.1875 lb ai/acre (filberts) for a single application (BEAD 2007) with a seasonal maximum label rate of 3.0 lb ai/acre (cherries). For non-agricultural uses on Christmas trees, ornamental and/or shade trees, ornamental herbaceous plants, ornamental non-flowering plants, ornamental woody shrubs and vines, the current labels do not specify a maximum annual application rate nor the maximum number of single applications allowed. For those uses, the application rates are provided in gallons of the product per pot and/or in lb of active ingredient per 100 gallons. Therefore, assumptions of how many pots per acre are treated etc. will be made unless additional information is available.

6. ENVIRONMENTAL FATE SUMMARY

6.1 Active Ingredient

The major pathways of triflumizole degradation appear to be hydrolysis under acidic and alkaline conditions (8.9 days at pH 5.0; 3.9 days at pH 9.0), photolysis (2-3 days), and to lesser extent aerobic soil metabolism. Triflumizole is not likely to be persistent under most environmental conditions. It is unlikely to be very mobile except for soils in a sand textural class with low organic material. Based on the laboratory and field study findings it has low potential to reach groundwater but it will reach surface water in both the dissolved form and sorbed onto soils and organic material for several weeks following application.

Triflumizole is converted to several degradates containing the 4-chloro-2-trifluoromethyl aniline moiety during hydrolysis, photolysis as well as during aerobic soil metabolism. During the HED MARC meeting on February 26, 2002, the MARC committee has not excluded the possible toxicological concern for the metabolites containing the 4-chloro-2-trifluoromethyl aniline moiety.

Triflumizole photolyzed relatively rapidly under simulated sunlight conditions in water buffered to pH 7 and on the surface of soil with half-lives from 2 to 3 days. Triflumizole hydrolyzed in buffered water with calculated half-lives of 8.9, 64.6 and 3.9 days at pH 5, 7 and 9, respectively. The major degradate of hydrolysis was found to be 4-chloro-alpha-alpha-alpha-trifluoro-N-2-propoxyacetyl-o-toluidine (FD-1-1). No photolysis and hydrolysis data are available for triflumizole degradates.

In a laboratory aerobic soil metabolism study, triflumizole degraded with a half-life of 18 days. The major soil metabolite was identified as 2-trifluoromethyl-4-chloroaniline (FA-1-1) with minor metabolites comprising of 4-chloro-2-trifluoromethyl-propoxyacetanilide and N-[4-

chloro-2-(trifluoromethyl)phenyl]imino-2-propoxyethyl amine. No soil metabolism data are available for triflumizole degradates.

Laboratory soil mobility studies (batch equilibrium and column leaching) indicate that triflumizole has slightly mobile to relatively immobile characteristics depending upon the type of soil and organic matter content. The reported K_D values for sand, sandy loam, silt loam, and clay soils were 1.5, 7.6-63.3, 25.4, and 79.4, respectively. The corresponding K_{OC} values for sand, sandy loam, silt loam, and clay soils were 289, 1286-1993, 4113, and 2812, respectively. The low K_D of 1.5 in the sandy soil (organic matter content <1%) suggests that triflumizole is mobile under those conditions. The batch equilibrium study on the degradate, 4-chloro-alpha-alpha-alpha-trifluoro-N-2-propoxyacetyl-o-toluidine (FD-1-1) suggests that it is more mobile than the parent compound (K_{OC}: 33.6-961.2 for the FD-1-1). However, field studies conducted on sand and sandy loam soils indicated that triflumizole and its metabolites did not leach in soil depths below 12 inches.

Laboratory findings for triflumizole are in agreement with field dissipation studies with regard to soil metabolism half-life (18 days) and abiotic degradation rates at similar environmental conditions (pH and photoperiod) in the laboratory. In a series of previously reviewed cropped and non-cropped terrestrial field dissipation studies (2 valid and 2 invalid), triflumizole dissipated with half-lives of less than 8 days following soil and foliar applications at 0.5 lb ai/acre. No triflumizole or degradates were found below the 6- to 12-inch soil layer. The major degradate found in all studies was N-[4-chloro-2-(trifluoromethyl)phenyl]imino-2-propoxyethylamine (FM-6-1) at 0.21 ppm. 2-trifluoromethyl-4-chloroaniline (FA-1-1) and 4-chloro-alpha-alpha-alpha-trifluoro-N-2-propoxyacetyl-o-toluidine (FD-1-1) were identified at <0.02-0.08 ppm. These studies indicate that triflumizole rapidly dissipated under field conditions similar to normal product use.

In two recently reviewed bare ground terrestrial field dissipation studies (California and North Carolina), triflumizole and triflumizole degradates, FA-1-1, FD-1-1, and FM-6-1 were studied, and results were reported as FA-1-1 total residues. Trifumizole was applied 8 times at 7-day intervals at a rate of 0.25 lbs. a.i./acre. Total residue half-lives (expressed as FA-1-1 equivalents) were estimated to be 102 days in the California study and 133 days in the North Carolina study. Triflumizole residues were not seen below the 6- to 12-inch soil layer and only at very low concentrations, equal to or slightly above the level of detection (LOD) or 0.01 ppm. Pan evaporation data were not supplied. Therefore, it is difficult to conclude that leaching below the 6- to 12-inch soil layer is unlikely because the site water balance may not have been conducive to promote leaching. The analytical method selected did not permit the determination of individual species, parent and each degradate. However, these data and the data from the previous terrestrial field dissipation studies might suggest that triflumizole dissipates rather quickly, but triflumizole degradates may be more persistent based on the longer half-lives for the combined residue studies.

Triflumizole appears to accumulate in fish. BCFs for edible, nonedible, and whole fish were 107x, 758x, and 393x, respectively.

6.2 Total Residues

The half-lives for aerobic soil metabolism, hydrolysis and photolysis were calculated collectively for the parent and the degradates of concern which are the metabolites containing the 4-chloro-2-trifluoromethyl aniline moiety (Appendix 1). The half-lives derived for aquatic photolysis, soil photolysis and aerobic soil metabolism for total residues (parent and its degradates) correspond to 12.7 days, 8 days and 44 days, respectively. These data suggest that triflumizole and triflumizole degradates are moderately persistent in the environment. The total residue levels during hydrolysis at all pH conditions are very stable (half-life of several months to years). However, in the environment the microbial degradation pathways might have a greater influence than the non-biotic pathways and therefore, the total residues appear moderately stable in the environment.

The registrant submitted a mobility study for one of triflumizole degradates, FD-1-1. The degradate K_{OC} values suggest that it is more mobile than the parent compound. The K_D and K_{OC} values for FD-1-1 range from 0.178-13.8 and 33.6-961.2, respectively.

In the risk assessment, in modeling aquatic EECs, the PRZM/ EXAMS input parameters will be used for a total residues (triflumizole and its degradates). Detailed information on how the individual modeling input parameters were derived can be obtained from the "Tier I Estimated Drinking Water Concentrations for Triflumizole Including Degradates" memo (S. Ramasamy, March 3, 2002) (D281356). Detail information on the environmental fate and transport guideline studies submitted to EPA can be located in Appendix A of the "Section 3 request for uses of triflumizole on foliage for filberts" document (M. Janson and I. Maher, Feb. 7, 2006) (D312295).

7. ECOLOGICAL EFFECTS SUMMARY

Table 1 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 1. Taxonomic Groups and Most Sensitive Test Species Evaluated for Ecological Effects of Triflumizole.

Taxonomic group	Example(s) of representative species	Endpoint Used
Birds[a]	Bobwhite quail (*Colinus virginianus*) Mallard duck (*Anas platyrhynchos*)	Acute, LD_{50}/LC_{50} Chronic, NOAEC

Table 1. Taxonomic Groups and Most Sensitive Test Species Evaluated for Ecological Effects of Triflumizole.		
Taxonomic group	**Example(s) of representative species**	**Endpoint Used**
Mammals	Laboratory rat (*Rattus norvegicus*)	Acute LD_{50} NOAEC
Terrestrial insects	Honeybees (*Apis mellifera*)	Acute Oral LD_{50}
Freshwater fish[b]	Rainbow trout (*Oncorhynchus mykiss*) Fathead minnow (*Pimephales promelas*)	Acute LC_{50} Chronic NOAEC
Freshwater invertebrates	Water flea (*carinata*) Water flea (*Daphnia magna*)	Acute LC_{50} NOAEC
Estuarine/marine fish	Sheepshead minnow (Cyprinodon variegatus)	Acute LC_{50}
Estuarine/marine invertebrates	Mysid shrimp (*Mysidopsis bahia*) Eastern oyster (*Crassostrea virginica*)	Acute LC_{50} Acute EC_{50}
Terrestrial plants	Monocots – N/A Dicots – N/A	Seedling Emergence (Tier I or Tier II no EC_{25} estimated) Vegetative Vigor (Tier I or Tier II no EC_{25} estimated)
Freshwater vascular aquatic plants and algae	Duckweed *(Lemna gibba)*	Acute EC_{25} NOAEC
Freshwater non-vascular aquatic plants	Diatom *(Navicula pelliculosa)*	Acute EC_{25} EC_{05}
Estuarine/marine non-vascular aquatic plants	Diatom *(Skeletonema costatum)*	Acute EC_{50} EC_{05}

[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).

8. ECOSYSTEMS AT RISK

The ecosystems that could be potentially at risk due to agricultural use of triflumizole include terrestrial and aquatic (lakes, ponds, streams) habitats in proximity to triflumizole use areas. These habitats may be at risk from drift and/or runoff of triflumizole 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 triflumizole 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 triflumizole 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 triflumizole is generic and assumes that as a fungicide, triflumizole 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 triflumizole involve spray applications such as; ground, soil drench, aerial, microtube, high and low volume ground sprayers, hand held wand, dipper, mist sprayer and sprinkler irrigation of the pesticide to foliage and seeds (conifer and pineapple sections). Although not evident from the diagram, triflumizole degradation prior to runoff is explicitly considered. Runoff includes transport of triflumizole and its degradates in a dissolved state as well as triflumizole and its degradates 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 is proposed to 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 directly 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 (i.e., short grass, long grass, broadleaf plants etc.) will be assessed regardless of the type represented by the target crop, as a variety of food types will exist on and off the treated field.

In aquatic environment, once triflumizole 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. Degradations by abiotic hydrolysis, photolysis, and microbial mediated metabolism are taken into account. The route of exposure is uptake of triflumizole and its degradates dissolved in the water column through the gills and integument.

Triflumizole appears to accumulate in fish. BCFs for edible, nonedible, and whole fish were 107x, 758x, and 393x, respectively.

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

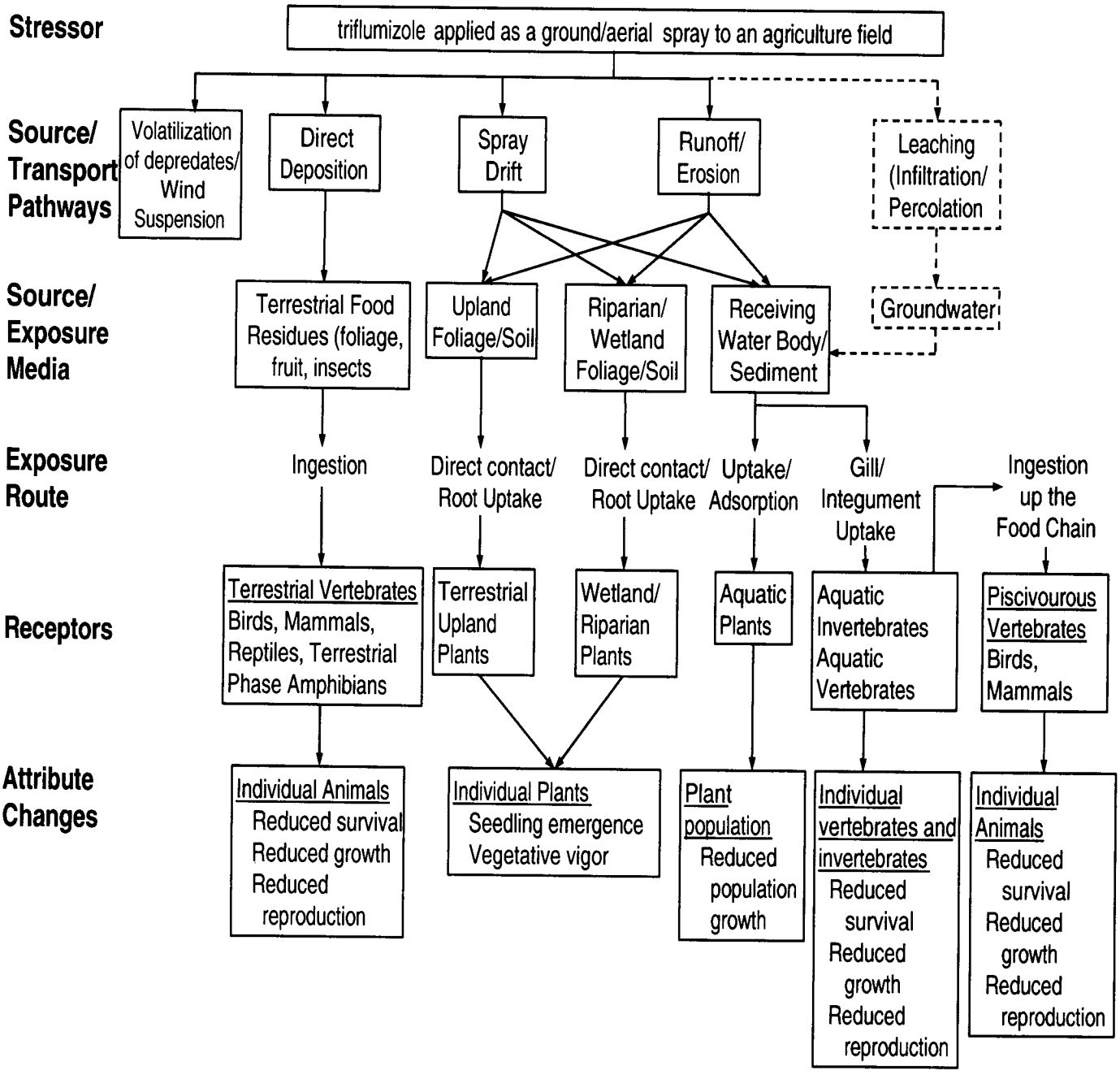


Figure 1. Conceptual model of the fate/transport and effects of triflumizole in the environment.

10. RISK HYPOTHESES

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

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 triflumizole 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 triflumizole drifts or moves with runoff to adjacent areas.

11.2. Measures of Effect

Aquatic plants and animals

(1) Freshwater Fish

Acute toxicity studies using TGAI for both bluegill *(Lepomis macrochirus)* sunfish and rainbow trout *(Oncorhynchus mykiss)* indicated that triflumizole is highly toxic to freshwater fish on an

acute exposure basis. Of the two species, the rainbow trout was more sensitive with an LC_{50} of 580 ppb compared to the blue gill sunfish LC_{50} of 1200 ppb. EFED used the LC_{50} of 580 ppb for evaluating acute risks to freshwater fish. The guideline requirement for 72-1c and 72-1a acute aquatic fish was fulfilled (ACC261211, ACC263361).

A freshwater fish early life-stage chronic toxicity test on fathead minnows *(Pimephales promelas)* was used to evaluate the chronic toxicity of triflumizole. Results from the study indicated a No Observed Adverse Effect Level (NOAEL) of 330 ppb based on wet weight of larvae. EFED used this value for evaluating chronic risk to freshwater fish. The guideline requirement for 72-4a for early life stage fish was fulfilled (MRID 40638301).

(2) Freshwater Invertebrates

A freshwater invertebrate acute toxicity study indicated that triflumizole is moderately toxic to waterfleas *(Daphnia carinata)*. The lowest estimated 48-hour EC50 was 1400 ppb. EFED will use this value for evaluating acute risk to freshwater invertebrates. The guideline requirement for acute freshwater invertebrates study (72-2a) was fulfilled (ACC073462).

An aquatic invertebrate life cycle test was conducted to evaluate the chronic toxicity of triflumizole to the freshwater aquatic invertebrate, *(Daphnia magna)*. The most sensitive endpoints were reproduction and terminal length (dry weight) with NOAECs of 67 ppb. EFED used the NOAEC of 67 ppb for reproduction and terminal length to evaluate chronic risk to freshwater invertebrates. The guideline requirement for freshwater invertebrate life cycle study (72-4b) was fulfilled (MRID 46302604).

(3) Estuarine/Marine Fish

Sheepshead minnows *(Cyprinodon variegatus)* were exposed to triflumizole under flow-through conditions for 96 hours to generate an estimate of the acute toxicity to an estuarine/marine fish. The estimated LC_{50} was 1400 ppb. The estimated LC_{50} classifies triflumizole as moderately toxic to estuarine and marine fish. Since the mean-measured concentrations tested did not produce a precise LC_{50} and no partial mortality was observed at concentrations lower than 1.7 mg ai/L (highest concentration treatment group) this study does not fulfill guideline requirements for an acute toxicity study with the Sheepshead minnow 72-3a and is classified as supplemental (MRID 46302601).

An estuarine/marine fish early life cycle test was conducted (MRID 46302605) to evaluate the chronic toxicity of triflumizole to estuarine and marine fish represented by sheepshead minnow. However this study was classified as invalid due to statistically-different values from solvent. Therefore, EFED will use the NOAEC of 80 ppb (acute to chronic ratio) to evaluate chronic risk to estuarine/marine fish. The guideline requirement for estuarine/marine fish early life cycle (72-4a) was not fulfilled. However, no further study for estuarine marine fish early life cycle is requested at this time.

(4) Estuarine/Marine Invertebrates

Two estuarine and marine invertebrate acute toxicity study indicated that triflumizole is highly toxic to eastern oyster *(Crassostrea virginica)* and mysid shrimp *(Americamysis bahia)* with LC_{50} of 720 ppb and LC_{50} of 600 ppb, respectively. The lowest estimated 96 hour-LC50 for estuarine/marine invertebrates was 600 ppb for mysid shrimp. EFED used this value for evaluating acute risk to estuarine/marine invertebrates. The guideline requirements for 72-3b and 72-3c for acute estuarine marine invertebrates was fulfilled (MRID 46302603 eastern oyster, MRID 46302602 mysid shrimp).

In a 96-hour acute toxicity study, cultures of the green alga, *(Selenastrum capricornutum)* were exposed to triflumizole at nominal concentrations. The 96-hour EC_{05} was reported to be 380 ppb based on all endpoints, which includes cell density and biomass. The 96-hour EC_{50} value based on biomass, the most sensitive endpoint was 630 ppb. This study fulfills guideline requirements for an acute toxicity study with green alga, *(Selenastrum capricornutum)* [123-2]Tier II and is classified as acceptable (MRID 46302607).

In a 96-hour acute toxicity study, cultures of the freshwater alga, *(Anabaena flos-aquae)* were exposed to triflumizole at nominal concentrations. The analysis detected significant reductions in cell density, growth rate, and biomass. The 96-hour NOAEC was 1600 ppb based on all endpoints. The 96-hour EC_{50} value based on biomass, the most sensitive endpoint, was 3000 ppb.The study is scientifically sound and satisfies the guideline requirements for a Tier II aquatic nonvascular plant study with the freshwater alga, *(Anabaena flos-aquae).* Consequently, the study is classified as acceptable (MRID 46302608).

In a 96-hour acute toxicity study, cultures of the marine diatom, *(Skeletonema costatum*) were exposed to triflumizole at nominal concentrations. The growth rate was the most sensitive endpoint, with an EC_{50} of 480 ppb. All endpoints were significantly reduced at all treatment levels, so the NOAEC was <0.083 ppb; the EC_{05} for growth rate was 180 ppb. Since the initial cell density of 77,000 cells/mL was greater than recommended (10,000 cells/mL), the study does not fulfill guideline requirements for a Tier II aquatic nonvascular plant study with the marine diatom, (Skeletonema costatum). Consequently, the study is classified as supplemental (MRID 46302609).

In a 7-day tier II acute toxicity study, freshwater aquatic vascular plants Duckweed, *(Lemna gibba)* , were exposed to triflumizole at nominal concentrations under static renewal conditions.. Frond number was the most sensitive endpoint, with an EC_{50} of 720 ppb. The corresponding NOAEC for this effect was 75 ppb. This study is scientifically sound and acceptable; the study satisfies the guidelines for an aquatic vascular plant study with Lemna gibba (MRID 46302611).

A tier II aquatic plant toxicity test, freshwater diatom *(Navicula pelliculosa),* indicated that biomass is the most sensitive endpoint to triflumizole at the concentrations tested. The estimated 120-hour EC_{50} was 140 ppb, based on biomass effects. The corresponding EC_{05} for this effect was 42 ppb. These endpoints will be used in the risk assessment. Based on these results, triflumizole is classified as practically non-toxic to diatom. This study is classified as acceptable (MRID 46302609).

An aquatic estuarine/marine invertebrate life cycle test was conducted to evaluate the chronic toxicity of triflumizole to estuarine/marine mysid. The most sensitive endpoint was sub-lethal delays in maturation with a NOAEC of 87 ppb. EFED used this value for evaluating chronic risk to estuarine/marine invertebrates. This study is scientifically sound. However, survival following pairing and terminal growth parameters was not reported in terms of gender. Therefore, this toxicity test, that utilized the estuarine/marine mysid did not fulfill the guideline requirement for 72-4c estuarine/marine invertebrate life cycle, and was classified as supplemental (MRID 46302606).

Terrestrial organisms

(1) Birds

An avian acute oral study was submitted for triflumizole indicated that the bobwhite quail *(Colinus virginianus)*, based on signs of toxicity, mortality, reduction of body weight gain and feed consumption was characterized as practically non-toxic to bobwhite quail. No mortality was reported at dosages less than 2510 mg/kg the highest dosage tested. The LD50 was determined to be >2510. This study will be used in this risk assessment and is classified as acceptable (ACC073462).

An avian dietary study was submitted for triflumizole indicated that the mallard duck (*Anas platyrhynchos)* based on reduction of body weight gain was characterized as practically non-toxic to mallard duck. No reduction of body weight gain was reported at dosages less than 5620 mg/kg the highest dosage tested. The LC50 was determined to be >5620. This study will be used in this risk assessment and is classified as Acceptable (ACC073462).

An avian dietary study was submitted for triflumizole indicated that the bobwhite quail *(Colinus virginianus)* based on mortality was characterized as practically non-toxic to bobwhite quail. No mortality was reported at dosages less than 5620 mg/kg the highest dosage tested. The LC50 was determined to be >5620 There appeared to be treatment related effects upon body weight gain and feed consumption at test concentrations of 1780 ppm and higher. This study will be used in this risk assessment and is classified as acceptable (ACC073462).

Two avian reproduction toxicity studies were submitted for triflumizole using the mallard duck *(Anas platyrhynchos)* and the bobwhite quail *(Colinus virginianus).* Both the mallard duck and a bobwhite quail were were exposed to Triflumizole using TGAI up to 1000 ppm ai and did not

produce any treatment- related effects for avian reproduction studies. The NOAEC was determined to be1000 ppm.

These studies will be in this risk assessment. Both the Mallard Duck and Bobwhite Quail studies MRIDs 40752009 and 40752010, respectively, and are classified as acceptable.

(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 triflumizole was evaluated using the common laboratory rat (Rattus rattus). The acute toxicity of triflumizole differed between male and female rats with males showing greater sensitivity. The LD_{50}s were 1057 and 1780 mg/kg-bw for males and females, respectively. For the assessment, the lower male-specific value of 1057 mg/kg will be used. This study was classified as acceptable (MRID 00144463).

For chronic toxicity data, a three-generation reproductive/developmental study on rats was selected for the risk assessment, with NOAEC of 30 ppm and NOAEL of 1.5 mg/kg-bw. The NOAEL value was used in the mammalian chronic risk assessment.

(3) Terrestrial Invertebrates

Acute toxicity of triflumizole to terrestrial invertebrates was assessed in studies where honeybees *(Apis mellifera)* were exposed with a 48-hour contact $LD_{50} > 160$ micrograms per bee (highest dose level tested). Therefore, triflumizole is considered practically non-toxic to honey bees on an acute oral contact basis. This study was classified as acceptable (ACC073462).

(4) Terrestrial Plants

Tier I and Tier II plant studies were submitted in support of the registration of triflumizole Tier I studies are aimed at quickly evaluating the phytotoxicity of a compound at the maximum single application rate which, for triflumizole, is 0.5 lbs a.i./A. Tier II plant studies are triggered when effects from the Tier I studies exceed 25% of the control. Although the Tier I seedling emergence and vegetative vigor studies did not exceed 25% of the control, the registrant still submitted Tier II studies for seedling emergence and vegetative vigor. There were no seedling emergence or vegetative vigor exceedences in either tier I or tier II studies with an application rate of 2 lbs ai/acre triflumizole per year, however, ryegrass had a 23% reduction in biomass with

no observed NOEC in the tier I study. However, at this time no further studies will be requested for terrestrial plants.

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 2 and Table 3.

Table 2. Summary of terrestrial assessment endpoints and proposed measures of effects for the screening level risk assessment of Triflumizole.

Assessment Endpoint	Measurement Endpoint
Avian Survival	Northern bobwhite quail Colinus virginianus LD_{50} > 2510 mg/kg BW
Avian Reproduction and/or Survival	Northern bobwhite quail Colinus virginianus NOAEC 1000 mg/kg diet
Mammalian Survival	Laboratory rat Rattus rattus 1057 mg/kg BW
Mammalian Reproduction and/or Survival	Laboratory rat Rattus rattus NOAEC 30 mg/kg/diet
Non-target Beneficial Insect Survival	Honey bee Apis meliferus >160 µg a.i./L
Terrestrial Plants Survival and Growth	Seedling Emergence Monocots (tier 1 and tier II) NOEC/<4.50 (2 lb ai/A) (no species in either tier I or tier II experienced inhibition greater than 25%
	Seedling Emergence Dicots (tier 1 and tier II) N/A (no species in either tier I or tier II experienced inhibition greater than 25%

Table 2. Summary of terrestrial assessment endpoints and proposed measures of effects for the screening level risk assessment of Triflumizole.	
Assessment Endpoint	Measurement Endpoint
	Vegetative Vigor Monocots (tier 1 and tier II) EC_{25}>4.50/ NOEC 4.50 (2 lb ai/A)
	Vegetative Vigor Dicots (tier 1 and tier II) EC_{25}>4.50/ NOEC4.50 (2 lb ai/A)

Table 3. Summary of aquatic assessment endpoints and proposed measures of effects for the screening level risk assessment of Triflumizole.	
Assessment Endpoint	Measurement Endpoint
Freshwater Fish Survival	Rainbow trout Oncorhynchus mykiss (TGAI) LC_{50} 580 ppb
Freshwater Fish Reproduction an/or Survival	Fathead Minnow Pimephales promelas (TGAI) NOAEC 33 ppb
Freshwater Invertebrate Survival	Water flea Daphnia carinata (TGAI) EC_{50} 1400 ppb
Freshwater Invertebrate Reproduction and/or Survival	Daphnia magna NOAEC 67 ppb
Marine/Estuarine Fish Survival	Sheepshead minnow LC_{50} 1400 ppb
Marine/Estuarine Fish Reproduction and/or Survival	NOAEC 80 ppb using acute to chronic ratio due to lack of submitted data
Marine/Estuarine Invertebrate Survival	Eastern oyster Crassostrea virginica EC_{50} 720 ppb Mysid shrimp

Table 3. Summary of aquatic assessment endpoints and proposed measures of effects for the screening level risk assessment of Triflumizole.	
Assessment Endpoint	Measurement Endpoint
	Americamysis bahia EC_{50} 600 ppb
Marine/Estuarine Invertebrate Reproduction and/or Survival	Mysid shrimp Americamysis bahia NOAEC 87 ppb
Aquatic Vascular and Non-vascular Plant Survival and Growth	Diatom (Navicula pelliculosa) [Tier II] 0.14/0.042(EC05)* 140 ppb used as endpoint Diatom (Skeletonema costatum) [Tier II] 0.48/0.18(EC05)* 480 ppb used as endpoint Duckweed (Lemna gibba) [Tier II]0.72/0.075 720 ppb used as endpoint

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

Table 4, below, identifies fate and ecological studies, which are missing or are not acceptable, and may be requested to assess risk to the environment:

Table 4. 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 risk study for estuarine/marine fish that was determined invalid due to statistically-different values from solvent	Study not requested	Acute to chronic ratios will be sufficient to not request study.
Marine diatom	Supplemental study because the initial cell density was greater than required.	Additional study not requested	This taxa (marine diatom) represented the most sensitive species for non-vascular plants.

Anaerobic aquatic metabolism study	Study was not submitted	Study not requested	Default value used in aquatic modeling did not trigger any LOC exceedance for aquatic organisms
Aerobic aquatic metabolism study	Study was not submitted	Study not requested	Default value used in aquatic modeling did not trigger any LOC exceedance for aquatic organisms
Foliar dissipation residue data	Foliar dissipation data studies or related data could potentially influence the modeling results since mammals exceeded Agency LOCs.	Propose to request the study or any available data relating to foliar dissipation rate	A default foliar dissipation rate of 35 days will be used in the modeling in place of the data if study is not submitted. Triflumizole degrades with half-lives less than 10 days under hydrolysis and photolysis (water and soil) and 18 days in aerobic soil metabolism study. This tend to indicate that foliar dissipation half life may be shorter than 35 days

The terrestrial and aquatic organism toxicity database for triflumizole is complete with ethe xception of a chronic risk study for estuarine/marine fish study that was determined invalid due to statistically different values from solvent. However, an acute chronic ratio may be used to determine estuarine marine chronic risks in triflumizole assessment. The marine diatom study was determined to be supplemental due to an initial cell density of (77,000cells/mL) which was greater than the initial recommended cell density of (10,000cells/mL).

The fate and transport database for triflumizole is complete with the exception of the anaerobic soil metabolism study (162-2), aerobic and anaerobic aquatic metabolism studies (162-3, 162-4). The missing laboratory studies would be beneficial in characterizing the potential for triflumizole leaching to ground water or remaining in surface water at concentrations of ecological or human health concern, and proposed to be requested for future risk assessments. Although these studies may provide more accurate modeling concentrations and risk characterization, they do not seem to significantly impact the risk conclusions as presented in the EFED 2001 and 2006 risk assessments for cherries and filberts, respectively. Therefore, these studies will not be requested for the upcoming registration review. A foliar dissipation study or any related data, however, may be beneficial in characterizing and reducing uncertainties for chronic mammal LOC exceedance.

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 previous, prior to 2006, assessments. These data include: acute toxicity studies in estuarine/marine fish (72-3a) and invertebrates (72-3b, 72-3c), chronic study in estuarine fish (72-4c), chronic life cycle toxicity studies in invertebrates (72-4b, 72-4d), and the toxicity studies in aquatic (122-2/123-2) and terrestrial plants (122-1/123-1).

(b) Currently used models and triflumizole degradates were not included in all but one risk assessment (Sec 3 on filberts).

(c) Some uses and application type scenarios were not assessed for ecological risk. These scenarios include Christmas trees, conifer seed, grapes, pear, and pineapple seed.

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

Drinking water is not expected to be a risk issue to humans based on modeling rates 3 lb ai/acre per season. Detailed information on the drinking water modeling can be obtained from the "Tier I Estimated Drinking Water Concentrations for Triflumizole including Degradates" memo (S. Ramasamy, March 3, 2002).

14. SUMMARY OF RISK

Summary of Risks Identified for Use on Filberts and Cherries

Estimated LOC exceedences for triflumizole are summarized in Table 5 below. The risk conclusions are based on previously conducted risk assessments. The most recent risk assessment conducted on filberts (D312295, 2006) employed the current models used in the ecological risk assessment. Another risk assessment, which was conducted on cherries (D242426, 2001) used old modeling techniques and limited toxicity data. The label maximum application rate to filberts is 1 lb a.i./acre/year (0.25 lb a.i./acre applied four times every 10 days). The label maximum application rate to cherries is 3 lb a.i./acre/year (0.5 lb a.i./acre applied six times every 7 days), and is the highest triflumizole application rate to date.

Table 5. LOC exceedences for triflumizole from use on filberts and cherries.*										
Use	Endpoint	Birds	Mammals	Terr. Plants	Insects	FW fish	SW Fish	FW Inverts	SW Inverts	Aquatic Plants
Filberts	Acute									
	Reproductive		✓							
Cherries	Acute					✓++				
	Reproductive		✓							

* All risk conclusions are based on previously conducted risk assessments (D312295 and D242426)

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

Blank cells indicate no LOC exceedences

++ Exceeds acute endangered LOCs for freshwater fish using Tier I aquatic modeling. Risk is likely to be sustained with refined Tier II modeling.

Aquatic Organisms

Based on the Tier II (PRZM/EXAMS) modeling, the 2006 risk assessment on filbert showed no LOC exceedence for any aquatic organisms. The aquatic modeling was based on four aerial applications at a single rate of 0.25 lb ai/acre (lower than the current maximum label rate). Table 6 summarizes the triflumizole EECs (6.4 µg a.i./L (peak), 6.1 µg a.i./L (21-day), 5.8 µg a.i./L (60-day)) and the toxicity data used in the assessment on filberts.

Table 6. Aquatic EECs and RQs for triflumizole based on four 0.25 lb ai/acre applications per season (the max. label application rate to filberts).

Taxa	Toxicity	EEC*	RQ
FW Fish	Acute LC50: 580 µg./L	6.4 µg a.i./L (peak EEC)	RQ<LOC
	Chronic NOAEC: 33 µg./L	5.8 ug a.i./L (60-day EEC)	RQ<LOC
FW Invertebrate	Acute EC_{50}: 1.4 mg./L	6.4 µg a.i./L	RQ<LOC
	Chronic NOAEC: 67 µg/L	6.1 µg a.i./L (21-day EEC)	RQ<LOC
FW Vascular Aquatic Plants	Acute EC_{25}: 720 µg./L	6.4 µg a.i./L	RQ<LOC
	Chronic NOAEC: 75 µg/L (*Lemna gibba)*	6.4 µg a.i./L	RQ<LOC
FW Non-vascular Plants and Algae	Acute EC_{25}: 140 µg./L	6.4 µg a.i./L	RQ<LOC
	Chronic EC_{05} (NOAEC ++): 42 µg./L (*Navicula pelliculosa*)	6.4 µg a.i./L	RQ<LOC
Estuarine/Marine Fish	Acute LC_{50} 1.4 mg./L *(Sheepshead minnow)*	6.4 µg a.i./L	RQ<LOC
	Chronic NOAEC 80 µg./L**		RQ<LOC
Estuarine/Marine Invertebrates	Acute Eastern oyster EC_{50}: 720 µg./L Mysid shrimp, EC_{50}: 600 µg./L	6.4 µg a.i./L	RQ <LOC
	Chronic NOAEC: 87 µg./L *(Americamysis bahia)*	6.1 µg a.i./L	RQ <LOC
Estuarine/Marine Mollusc	Acute LC50: 720 µg./L	6.4 µg a.i./L	RQ<LOC
	Chronic NOAEC: unavailable		
Estuarine/Marine Non-vascular Plants and Algae	Acute EC_{25}: 480µg./L	6.4 µg a.i./L	RQ<LOC
	Chronic EC_{05} (NOAEC ++): 180µg./L (*Skeletonema costatum*)	6.4 µg a.i./L	RQ<LOC

* Derived for four 0.25 lb a.i./acre aerial application every 10 days (filberts)
** Chronic NOAEC derived using acute to chronic ratio due to lack of submitted data.
++ Data not available

Based the Tier I (GENEEC) modeling, the 2001 risk assessment for cherries and ornamentals (maximum label use rate of 3 lb a.i./acre per season) showed slight LOC exceedance to fresh water fish endangered species on an acute basis (RQ = 0.09). However, EFEED believes that this risk is unlikely to be sustained if Tier II PRZM-EXAMS modeling is performed based on the use region's climate and the fate properties of triflumizole. Therefore, risks to aquatic organisms are not expected from uses on cherries and ornamentals and also from apples and pears (maximum label use rate of 2 lb a.i./acre per season).

Terrestrial Organisms

Acute and chronic RQs were not calculated for birds from uses on filberts. However, because the LD_{50} bw (>2510 ppm) and LC_{50} (>5620 ppm) diet were greater than the highest dosage administered for bobwhite quail, triflumizole was characterized as practically non-toxic to birds. No acute and chronic risks were assumed in the 2001 risk assessment for cherries and ornamentals, and in the 2006 risk assessment for filberts.

No LOCs were exceeded for mammals across all weight classes based on a maximum seasonal application rate of 1 lb a.i./acre and the scenarios modeled in the 2006 assessment. The acute RQs range from 0.07 to <0.01 and are shown in Table 7. Based on these RQs, it is expected that application rate of 2 - 3 lb a.i./acre per season will result in some acute LOC exceedance for mammals, especially those feeding on short grass, tall grass, and broadleaf plants/small insects.

Table 7. Mammalian dose-based acute RQ values for proposed uses of triflumizole based on a rat LD_{50} = 1057 mg/kg-bw and upper-bound Kenaga values.

Use/App. Method	Application Rate lbs a.i./A (#app/interval in 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
Filberts	0.25 lb ai/A (4/10)	15	0.07	0.03	0.04	<0.01	<0.01
		35	0.06	0.03	0.04	<0.01	<0.01
		1000	0.03	0.02	0.02	<0.01	<0.01

Chronic LOCs were exceeded for 15g, 35g and 100g mammals that consume short grass, tall grass, broadleaf plants/small insects and fruits/ pods/large insects with chronic RQs ranging from 0.34 to 53 for upper-bound Kenaga residues (Table 8). The chronic RQs were also exceeded for mean Kenaga values as shown in Table 9. It is therefore expected that higher application rate use scenarios will result in even greater chronic RQs exceedences for mammalian organisms, possibly including mammals feeding on seeds.

Table 8. Mammalian dose-based chronic RQ values for proposed use of Triflumizole based on a rat NOAEL 1.50 of mg/kg/day and upper-bound Kenaga residues.

Use/App Method	Application Rate lbs a.i./A (#app/interval in days)	Body Weight [g]	Mammalian Chronic Risk Quotients (upper-bound Kenaga residues)				
			Short Grass	Tall Grass	Broadleaf Plants/Small Insects	Fruits/pods/ large insects	Seeds
Filberts	0.25 lb ai/A (4/10)	15	* 52.84	* 24.22	* 29.72	* 3.30	0.73
		35	* 45.14	* 20.69	* 25.39	* 2.82	0.63
		1000	* 24.20	* 11.09	* 13.61	* 1.51	0.34

* exceeds LOCs for chronic risk to mammals (RQ >1.0)

Table 9. Mammalian dose-based chronic RQ values for proposed uses of triflumizole based on a rat reproductive NOAEL of 1.50 mg/kg-bw/day and mean Kenaga values.

Use	Application Rate lbs. a.i./A (# app / interval, days)	Body Weight, [g]	Mammalian Chronic Risk Quotients (based on mean Kenega residues)				
			Short Grass	Tall Grass	Broadleaf Plants/Small Insects	Fruits/pods/ large insects	Seeds
Filberts	0.25 (4 / 10)	15	*18.65	* 7.90	* 9.87	* 1.54	0.34
		35	* 16.01	* 6.78	* 8.48	* 1.32	0.30
		1000	* 8.41	* 3.56	* 4.45	0.69	0.14

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

Seedling emergence and vegetative vigor RQs were not calculated for terrestrial plants for uses on filberts because no species in either Tier I or tier II experienced inhibition greater than 25%. Therefore, an EC_{25} was not determined. Ryegrass experienced 23% reduction from control in Tier I. However, EC_{05} was not determined for ryegrass. Uncertainty exists with ryegrass for endangered species, but since the Tier II NOAEC's for all monocots and dicots were equivalent to the maximum concentration of 4.50 (kg ai/ha) or 2 lb ai/A, it is unlikely that the RQ for endangered species for monocots will exceed the LOC at 0.25 lb ai/A/event (filbert) or at 0.5 lb ai/A/event (cherries). The RQ for dicots did not exceed the LOC for endangered species.

15. RESIDUES OF TRIFLUMIZOLE AND TRIFLUMIZOLE DEGRADATE IN WATER

Submitted studies suggest that triflumizole dissipates rather quickly, not likely to be persistent under most environmental conditions and, except for soils in a sand textural class with low organic material, unlikely to be very mobile. Triflumizole degradates may be more persistent based on the longer half-lives for the combined residue studies, thus, the total residues are considered moderately stable in the environment. The major degradate's (FD-1-1) K_{OC} values suggest that it is more mobile than the parent compound, the K_D and K_{OC} values range from 0.178-13.8 and 33.6-961.2, respectively.

Triflumizole may drift off during application and runoff into the surface water, but less likely reach ground water. After application, total residues may runoff into the adjacent surface water and may potentially reach shallow ground water. In the field dissipation studies, triflumizole residues will not leach below the 6- to 12-inch soil layer. However, the pan evaporation data were not supplied, therefore, it is difficult to conclude that leaching below the 6- to 12-inch soil layer is not likely.

From the registered uses, triflumizole maximum application rate is for cherries, i.e. 0.5 lb ai/acre applied six times every seven days. For the maximum application rate on cherries, the acute (peak) estimated drinking water concentration is 191 ppb and the chronic (annual average) estimated drinking water concentration is 40 ppb for surface water. The acute and chronic ground water screening concentration is 0.12 ppb. The estimated concentrations represent the degradates containing the 4-chloro-2-trifluoromethyl aniline moiety namely, FD-1-1, FM-6-1, FA-1-1, FM-5-1, FM-3-1, FD-2-1, and FM-8-1, along with the parent compound. The drinking water concentrations for cherries were estimated via Tier I modeling (FIRST and SCI-GROW), which provide high-end estimates of water concentrations for human health risk assessment. These water concentrations are not expected to exceed HED's level of concern and their refinement using the Tier II PRZM/EXAMS modeling is not anticipated.

Detailed information on the drinking water modeling can be obtained from the "Tier I Estimated Drinking Water Concentrations for Triflumizole including Degradates" memo (S. Ramasamy, March 3, 2002).

16. OTHER INFORMATION NEEDS

There is specific information that will assist the Agency in refining the ecological risk assessment, including any species-specific effects determinations. The Agency is very much interested in obtaining the following information:

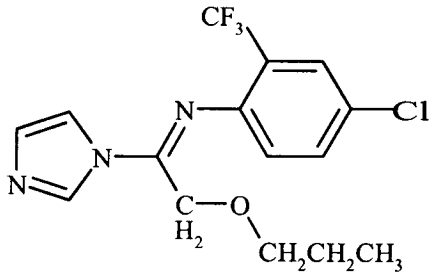
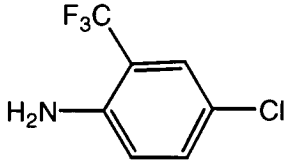
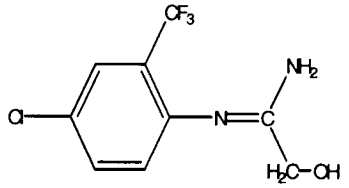
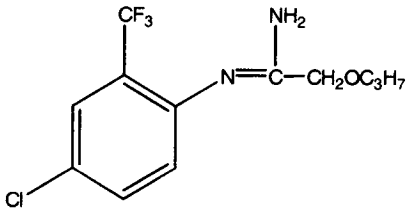
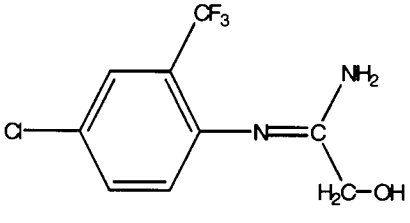
12. confirmation on the following label information
    a. sites of application
    b. formulations
    c. application methods and equipment
    d. maximum application rates
    e. frequency of application, application intervals, and maximum number of applications per season
    f. geographic limitations on use
13. use or potential use distribution (e.g., acreage and geographical distribution of relevant crops)
14. use history
15. median and 90th percentile reported use rates (lbs ai/acre) from usage data – national, state, and county
16. application timing (date of first application and application intervals) by crop – national, state, and county
17. sub-county crop location data
18. usage/use information for non-agricultural uses (e.g., forestry, residential, rights-of-way)
19. 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 90th 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

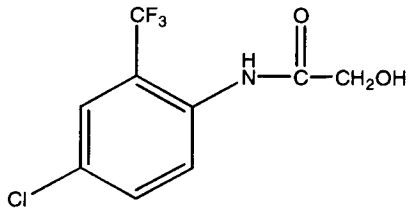
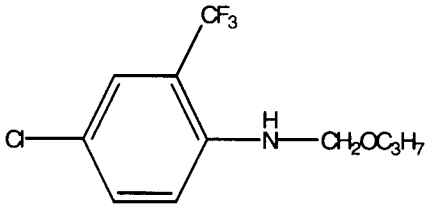
20. typical interval (days)
21. state or local use restrictions
22. ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency
23. monitoring data

The analysis plan will be revisited and may be revised depending upon the data available in the open literature and the information submitted by the public in response to the opening of the Registration Review docket.

Appendix 1: Table 1. Chemical name and structure of triflumizole and its degradates of potential concern

Common Name/Number	Chemical Structure
Triflumizole [1-(4-chloro-2-(trifluoromethyl)phenyl) imino-2-propoxyethyl]-1*H*-imidazole	
Metabolite FA-1-1 4-chloro-2-trifluoromethylaniline moiety	
Metabolite FM-5-1 (E)-N-(4-chloro-α, α, α-trifluoromethylphenyl-N-formyl)-propoxyacetamidine	
Metabolite FM-6-1 N-(4-chloro-2-trifluoromethyl-phenyl)-imino-1-propoxyethylamine)	
Metabolite FM-8-1 N-(4-chloro-2-trifluoromethyl-phenyl)-imino-2-methonolamine	

Appendix 1: Table 1. Chemical name and structure of triflumizole and its degradates of potential concern

Common Name/Number	Chemical Structure
FD-2-1 4-chloro-2-trifluoromethylphenyl-hydroxyacetanilide	
Metabolite FD-1-1 N-(4-chloro-2-trifluoromethylphenyl)-2-propoxyacetamide or (4-chloro-2-trifluoromethyl-propoxyacetanilide)	

IV. HUMAN HEALTH EFFECTS SCOPING DOCUMENT

(found on next page)

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

March 22, 2007

SUBJECT: **Triflumizole** (PC 128879) Health Effects Division (HED) Scoping Assessment for Registration Review

FROM: Catherine Eiden, Chief
Danette Drew, Senior Scientist
Reregistration Branch 3
Health Effects Division (7509P)
Office of Pesticide Programs

TO: Mark T. Howard, Chemical Review Manager
Reregistration Branch
Special Review and Reregistration Division (7508P)
Office of Pesticide Programs

Attached is the HED scoping assessment for the chemical triflumizole.

Summary Findings and Anticipated Work. Triflumizole was registered in 1989 on apples, pears, grapes, and as a result tolerances were established for these food commodities and for livestock commodities. Subsequent permanent registrations followed for hazelnuts/filberts, imported greenhouse tomatoes, strawberries, cherries, and cucurbits. In addition, several Section 18 registrations have been requested and granted. The HED human health risk assessments reflect these registrations and uses of triflumizole. The toxicity and exposure databases are adequate to support these human health risk assessments and make safety findings under the Food Quality and Protection Act (FQPA). 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). Potential residential exposures to triflumizole are possible. Although not intended for homeowner use, there are no restrictions on triflumizole labels to prevent homeowners from applying triflumizole on ornamentals. Potential risks associated with exposures of homeowners applying triflumizole to ornamentals are not of concern. Potential post-application exposures have been determined to be negligible. These risk estimates are generally conservative and health-protective and should not underestimate exposure and risk.

Occupational risk assessments for most of the registered uses reflect current policy and practice, do not exceed levels of concern, and do not need revision. No new data are required.

HED anticipates some minor revisions to the triflumizole risk assessments. The current hazard characterization does not adequately reflect available findings from reviewed neurotoxicity studies and their impact on the reserved developmental neurotoxicity study (DNT) requirement, or the current status of the 28-day inhalation study requirement, which has been waived. The hazard characterization should be updated to reflect these findings and decisions. HED will review the occupational risk assessments and determine whether revised worker risk assessments are needed for grapes and pineapple seed pieces. Finally, HED notes that the tolerance on filberts referred to as "time-limited" in the risk assessments has been converted to a permanent tolerance.

Introduction. Triflumizole was first registered in 1989 and as a result was not subject to review under the reregistration process recently completed under FIFRA and 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. In response to the Registration Review process recently initiated, the team for triflumizole has taken the following steps to determine the current status of the human health risk assessment for triflumizole:

- 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 triflumizole 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 180.476
- 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

Use Pattern. Triflumizole is a broad spectrum foliar fungicide used to control plant diseases by inhibiting ergosterol biosynthesis in fungi. It treats powdery mildew, leaf spot, scab and various blights, rusts and rots. It is registered for use on hazelnuts, pome fruits, leafy and cucurbit vegetables, grapes, strawberries, and cherries, ornamentals in greenhouses/shadehouses, interiorscapes, and Christmas trees/conifers on nurseries and plantations. It is used as a pre-plant seed piece treatment on pineapples. Triflumizole can be applied to trees, shrubs, and vines. There are no registrations on turf. There are no garden vegetable uses.

Hazard Characterization and FQPA Safety Factor. The toxicity database for triflumizole was reviewed in 2002 and found to be substantially complete and adequate to assess risk under FQPA. The current risk assessments reflect the removal of the FQPA Safety Factor (reduction to 1X), and removal of an additional uncertainty factor for insufficiencies in the database. Even though there have been changes in the policies used to determine an appropriate FQPA Safety Factor since 2001, HED believes the FQPA Safety Factor reflected in the current risk assessment for triflumizole is supported by the available toxicity and exposure information on triflumizole.

The database includes acceptable studies on developmental, reproductive/fertility, neurotoxic, subchronic, chronic, carcinogenic, and mutagenic effects, as well as information on the metabolism and pharmacokinetics of triflumizole. A special study on hepatic enzyme induction is also available. A search of the open literature was conducted for toxicity studies involving triflumizole using NIH's PubMed, and Google Scholar. No *in vivo* toxicity testing studies relevant to HED's human health risk assessments were found. No new toxicity data have been submitted and no new toxicity data are required.

The liver is the primary target organ for triflumizole. Liver effects were seen in subchronic and chronic/carcinogenicity studies in rats, mice, and dogs. Dogs appeared to be less sensitive to the effects than rodents. A special microsomal induction study showed that triflumizole did induce microsomal enzymes in the liver at high doses. Body weight effects were noted across studies. Cystic or hyperplastic lesions in the endocrine glands and lymph nodes were noted at the highest dose tested in the chronic rat study.

Signs of neurotoxicity were seen in the acute oral and inhalation studies in the rat and mouse. These effects triggered the application of a database uncertainty factor (UF_{db}) of 3X for lack of acute and subchronic neurotoxicity studies. A developmental neurotoxicity study was placed on "reserve" pending the results of the acute and subchronic studies. Clinical signs of neurotoxicity were noted in the acute neurotoxicity study at mid and high doses. As a result, the endpoint from this study was used to assess acute dietary risks from one-day exposures to triflumizole in the diet of the general population. No evidence of neurotoxicity was seen in the submitted subchronic neurotoxicity study. The 3X UF_{db} was subsequently removed (reduced to 1X) when the studies were submitted, reviewed, found to be acceptable, and used in the current risk assessments to protect against neurotoxic effects. The submitted acute and subchronic neurotoxicity studies were considered sufficient to address concerns related to neurotoxic effects; consequently, a DNT study is not needed.

No special sensitivity in rat and rabbit offspring was noted as a result of post-natal exposures to triflumizole. Adult animals and their offspring exhibited similar responses to the same doses of triflumizole. Similarly, adult animals and their fetuses exhibited effects at the same doses, but the effects in the fetuses were considered more severe than those in the adults. This *qualitative* susceptibility was noted *in utero* in a rat developmental study. To address any special sensitivity in the developing fetus, the endpoint from the developmental study in the rat was used in the acute dietary risk assessment for females of child-bearing age. As a result, the FQPA Safety Factor was removed (reduced to 1X).

Additional toxic endpoints were selected for risk assessments based on chronic dietary, incidental oral, dermal, and inhalation exposures.

Triflumizole is currently classified as a "Group E " carcinogen, i.e., based on the evidence presented in two animal species (rat and mouse) there is no evidence for carcinogenicity in humans. It shows no evidence of being mutagenic in *in vitro* and *in vivo* studies.

In March 2002, a 28-day inhalation study was identified as a data gap. Since then, HED has implemented an inhalation toxicity study waiver policy. Since triflumizole is not volatile, is classified as a Category IV inhalation toxicant, has risk estimates for inhalation exposures that are negligible, and exhibits negligible droplets of inhalable size under normal agricultural conditions of use, it meets all four criteria outlined in the policy. Subsequently, a waiver request for the 28-day inhalation toxicity study was granted (September 2004) and the requirement for a 28-day inhalation study has been removed.

No additional toxicity data for triflumizole are required.

Dietary Exposures and Risks. Dietary risk estimates for exposures to triflumizole 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), Section 18 Emergency Exemption uses resulting in time-limited tolerances on parsley, dandelion, Swiss chard, collards, kale, kohlrabi, mustard greens, Chinese napa cabbage, broccoli, cilantro, turnip greens, and an import tolerance on tomatoes. 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.

Acute dietary risk at the 95th percentile of exposure for the general population was estimated to be 9.3% of the acute Population Adjusted Dose (aPAD), 25% of the aPAD for children 1 to 2 years old, and 17% of the aPAD for females of child-bearing age. Acute dietary exposures were estimated using tolerance level residues and assuming 100% of the crop treated under a Tier 1 assessment.

Chronic dietary risk for the general population was estimated to be 17% of the chronic Population Adjusted Dose (cPAD) and 31% of the cPAD for children 1 to 2 years old. Chronic dietary exposures were estimated using anticipated residues based on average field trial data for apple, pear, cherry, grapes, strawberry, cucurbit , and milk commodities. Percent crop treated information was used for apple, pear, and grapes. For all other commodities in the assessment tolerance level residues and 100% crop-treated values were assumed.

Drinking water exposures were assessed for cherries using direct incorporation of estimated environmental concentrations (EECs) into dietary acute and chronic analyses, respectively, and reflect current policy and practice.

Although not used in the dietary risk assessments, monitoring data from the USDA's Pesticide Data Program (PDP) for the three most current years (2003 - 2005), indicate very few detections of triflumizole on the crops tested. Between 2003 and 2005, approximately 7000 samples of crops representative of the registered uses of triflumizole were analyzed. In 2004 and 2005 three samples of strawberries had detectable residues below the tolerance. These data may be used to refine the triflumizole dietary risk assessment if refinement is warranted in the future. Current percent crop-treated information (March 2006) is available from BEAD and could be used to refine the dietary assessments, if future uses result in risks of concern based on the assumption of 100% crop-treated.

The dietary exposure assessments based on food are conservative assuming tolerance or field trial level residues and 100% crop-treated for many commodities, though not all. The dietary exposure assessments based on drinking water utilize water concentrations of triflumizole generated by a Tier I surface water runoff model, which is designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded. The current dietary risk assessments are not expected to underestimate risks.

Residential Exposures and Risks. Triflumizole is registered for use on ornamental plants grown in the following areas: greenhouses and shadehouses, nurseries, including Christmas trees/conifer plantations, and interiorscapes. This may include applications to trees, shrubs, and vines around residences. Though not a restricted use pesticide, the product is intended for "commercial" use rather than "private residential" use. There are no registered uses on lawns or turf. There are no registered garden uses of triflumizole.

Although homeowners are not expected to apply triflumizole, there are no restrictions on the labels to prevent a homeowner from buying and applying it. Consequently, HED has reviewed the occupational assessment for commercial applicators making applications to trees, shrubs, and vines and determined that risk estimates are below levels of concern. HED believes that any potential homeowner exposure as a result of the application of triflumizole products would be addressed by the occupational risk assessment, and also not be of concern. Potential incidental exposures of homeowners to residues of triflumizole after its application on trees, shrubs, and vines were considered by the HED Exposure Scientific Advisory Council (EXPO SAC) and determined to be negligible. Consequently, no residential risk assessments for post-application

exposures were conducted. Risk estimates based on potential residential exposures are not of concern.

Aggregate Exposures and Risks. Risk estimates for aggregate exposures to triflumizole are below levels of concern. In the current assessment, one-day exposures to triflumizole in food and drinking water were combined and compared to the appropriate endpoint to estimate acute aggregate risk. Average exposures to triflumizole in food and drinking water were combined and compared to the appropriate endpoint to estimate chronic aggregate risk. Since the potential for residential exposures to triflumizole are negligible, short- and intermediate-term dermal, inhalation, and incidental oral exposures were not aggregated with dietary exposures.

Cumulative Risk Assessment. The Agency has not determined whether triflumizole 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 triflumizole is determined to share a common mechanism of toxicity with other substances, then methods for aggregating exposures and risks will be developed. Until triflumizole 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 triflumizole and other substances.

Occupational Exposures and Risks. Occupational risk assessments reflect current policy and practice for all currently registered uses of triflumizole with the exception of grapes and seed piece treatment for pineapples. Risk estimates for short-term exposures of pesticide handlers (mixers, loaders, applicators) are below the level concern, that is, Margins of Exposure (MOEs) are > 100.

- MOEs range from 2900 to 87,000 for cherries, apples, and pears
- MOEs range from 5900 to 40,000 for hazelnuts
- MOEs range from 21,000 to 46,000 for cucurbits
- MOEs range from 83,000 to 175,000 for strawberries
- MOEs range from 708 to 175,000 for ornamentals
- MOEs range from 278 to 11,0000 for leafy greens

Intermediate-term exposures to triflumizole are not anticipated for handlers.

Risk estimates for short-term and intermediate-term post-application exposures for harvestings/thinning/pruning activities are below the level concern, i.e., MOEs are > 100. Post-application exposures are not anticipated for ornamental applications.

- MOEs estimated to be 1700 for leafy greens
- MOEs estimated to be 541 for cherries, apples, pears, and hazelnuts

- MOEs estimated to be 231 for cucurbits and strawberries

Highly protective assumptions regarding the transfer of residues (transfer coefficients) and residues present on foliage on the first day after treatment were used in the risk assessments to estimate post-application exposures. The risk assessments are considered to be conservative and to provide screening- level estimates of exposure. Chemical-specific exposure data are not available for triflumizole and were not used in these assessments. The majority of the existing occupational risk assessments for triflumizole need not be revisited under Registration Review. However, worker risks associated with treatment of grapes and pineapple seed pieces will be revisited to ensure they reflect current policy and practice.

Poisoning Incidents Reports. Very few incidents of poisoning associated with triflumizole exposures have been reported. For the following databases, there were no reports of triflumizole poisonings: OPP's Incident Data System, and the Poison Control Center (1993 to 2003). 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. Out of the 5899 cases, one case was associated with the use of triflumizole. In 2003, a male applicator in the State of Washington reported contact dermatitis. These findings support HED's estimates of low risk associated with worker's exposures to triflumizole.

Tolerances. Permanent and time-limited tolerances listed below were taken from the most recent Code of Federal Regulations (CFR). In addition to those listed, a permanent tolerance of 1.5 ppm on *imported* greenhouse tomatoes was recommended by HED (May 2005). Pineapples are listed on triflumizole labels for pre-plant seed piece treatments. However, the HED Chemistry Science Advisory Council (1/20/04) determined that the use constituted a non-food/non-feed use and that no tolerance on pineapple was necessary.

§ 180.476 Triflumizole; tolerances for residues.

(a) *General.*

(1) Tolerances are established for the combined residues of the fungicide triflumizole, 1-(1-((4-chloro-2-(trifluoromethyl)phenyl)imino)-2-propoxyethyl)-1*H*-imidazole, and its metabolites containing the 4-chloro-2-trifluoromethylaniline moiety, calculated as the parent compound, in or on the following food commodities:

Commodity	Parts per million:
Apple, wet pomace	2.0
Apple	0.5
Cherry, sweet	1.5
Cherry, tart	1.5
Filbert	0.05
Grape	2.5
Grape wet and dried pomace	15.0

Grape, raisin, waste	10.0
Pear	0.5
Strawberry	2.0
Vegetable, cucurbit, Group 09	0.5

(2) Tolerances are established for the combined residues of the fungicide triflumizole, 1-(1-((4-chloro-2-(trifluoromethyl)phenyl)imino)-2-propoxyethyl)-1*H*-imidazole, the metabolite 4-chloro-2-hydroxy-6-trifluoromethylaniline sulfate, and other metabolites containing the 4-chloro-2-trifluoromethylaniline moiety, calculated as the parent compound, in or on the following food commodities of animal origin:

Commodity	Parts per million
Cattle, fat	0.5
Cattle, meat	0.05
Cattle, meat byproducts	0.5
Egg	0.05
Goat, fat	0.5
Goat, meat	0.05
Goat, meat byproducts	0.5
Hog, fat	0.5
Hog, meat	0.05
Hog, meat byproducts	0.5
Horse, fat	0.5
Horse, meat	0.05
Horse, meat byproducts	0.5
Milk	0.05
Poultry, fat	0.05
Poultry, meat	0.05
Poultry, meat byproducts	0.1
Sheep, fat	0.5
Sheep, meat	0.05
Sheep, meat byproducts	0.5

(b) *Section 18 Emergency Exemptions.*

Time limited tolerances are established for the residues triflumizole (1-(1-((4-chloro-2-(trifluoromethyl)phenyl)imino)-2-propoxyethyl)-1H-imidazole) and its metabolites containing the 4-chloro-2-trifluoromethylaniline moiety, calculated as the parent in connection with use of the pesticide under section18 emergency exemptions granted by
EPA. The tolerances are specified in the following table, and will expire and are revoked on the dates specified.

Commodity	Parts per million	Expiration/revocation date

Broccoli	1.0	12/31/09
Cabbage, chinese, napa	20.0	12/31/09
Collards	20.0	12/31/09
Coriander, leaves	20.0	12/31/09
Dandelion, leaves	7.0	12/31/09
Kale	20.0	12/31/09
Kohlrabi	20.0	12/31/09
Mustard, greens	20.0	12/31/09
Parsley, leaves	20.0	12/31/09
Swiss chard	7.0	12/31/09
Turnip, greens	20.0	12/31/09

(c) *Tolerances with regional registrations.*
[Reserved]

Tolerance Harmonization. The Codex Alimentarius Commission has not established Maximum Residue Limits (MRLs) for residues of triflumizole in/on various raw agricultural and processed commodities. Canada and Mexico have not established MRLs for triflumizole. However, Japan, Australia, and the Netherlands have set MRLs. Australia sets grapes and pome fruits at 0.5 ppm. The Netherlands currently sets tomatoes at 1 ppm, cucumbers at 0.2 ppm, and others at 0.05 ppm, but will defer to EU. Japan sets: apple, pear, grape, and strawberry at 2 ppm; cabbage, broccoli, cucumber (and other cucurbits), and squash, and a variety of leafy greens at 1ppm; melons at 2 ppm; and cherries at 3 ppm. They also list many other MRLs for a variety of crops (some are listed as provisional). US tolerances and MRLs from these countries do not appear to have been harmonized.

Other Considerations

None

Reference Memoranda:

Review of Triflumizole Incidents Reports, M. Hawkins, August 15, 2006.

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D325682, Triflumizole – Exposure/Risk Assessment for the FIFRA Section 18 Use of Triflumizole on Leafy Green Vegetables in Texas", M. Dow, February 1, 2006.

D316789, "Request for Permanent Tolerances for Residues of Triflumizole in/on Imported Greenhouse-Grown Tomatoes and Section 18 Specific Exemption for the Use of Triflumizole on Turnip Greens in Texas", J. Tyler et al., May 26, 2005

D306463, "Section 18 Specific Exemption for the Use of Triflumizole on Parsley, Dandelion, Swiss chard, Collards, Kale, Kohlrabi, Mustard greens, Chinese napa cabbage, Broccoli, and Cilantro", Tyler, et al., January 28, 2005.

D280864 and D280605, "Triflumizole in/on Strawberries, Cucurbit vegetables, Cherries, and Hazelnuts", J. Tyler et al., April 25, 2002.

D282644, "Triflumizole – Amendment to: Human Exposure and Risk Assessment for Proposed New Uses on Cherries, Hazelnuts, Cucurbits, Strawberries, Outdoor Ornamentals, and Institutional, Recreational and Residential Landscapes", M. Dow, April 26, 2002.

D306593, "Triflumizole – Waiver Request for 28-Day Inhalation Study", TXR 0053181, M. Dow, September 23, 2004.

Minutes of 9/17/03 Chem SAC Meeting. 1/20/04. Render a Food/Non-Food use Decision on the Proposed Use of Procure 50WS Fungicide to Treat Pineapple Seed Pieces.

"Triflumizole – Revised Report of the Hazard Identification Assessment Review Committee", TXR 0050571, March 19, 2002.

"Triflumizole – Report of the FQPA Safety Factor Committee", TXR 0050587, March 21, 2002.

D280867, "Triflumizole. Issues to be Presented to the Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Meeting on 2/26/02", J Tyler, February 26, 2002.

HED SOP 2002.01 Standard Operating Procedure – Waiver Criteria for Multiple-Exposure Inhalation Toxicity Studies. August 15, 2002.

V. 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)
SOP	Standard Operating Procedure
TGAI	Technical Grade Active Ingredient
USDA	United States Department of Agriculture
UF	Uncertainty Factor
WPS	Worker Protection Standard
WQ	Water Quality