Fomesafen Summary Document: Registration Review

March 2007

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Fomesafen Summary Document
Registration Review: Initial Docket
March 2007

Registration Review Document for Fomesafen

Case No. 7211

Approved by: Debra Edwards Date: March 22, 2007

Debra Edwards, Ph. D. Month Day, 2007
Director
Special Review and Reregistration Division

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I. Preliminary Work Plan - Fomesafen

Introduction:

The Food Quality Protection Act of 1996 mandated 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 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 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 intends to review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. The public phase of registration review begins when the initial docket is opened for each case. The docket is the Agency's opportunity to state 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 does not foresee requiring any additional ecological effects or environmental fate data to support the current assessments. However, the Agency anticipates conducting an endangered species risk assessment for all uses. The Agency anticipates that no additional human health risk assessments or related data will be needed.

Ecological Risk:

- Ecological risk assessments for fomesafen uses were completed January 30, 2006 for use on soybeans, and for new uses of fomesafen on cotton, snap beans, and dry beans.

- The Agency has not conducted a risk assessment that supports a complete endangered species determination.

Human Health Risk:

- The previously completed dietary assessments that considered dietary exposure to fomesafen from food and drinking water are adequate and there is no dietary risk that exceeds the Agency's level of concern (LOC). Thus, no additional data are needed.

- The occupational database is completed for the existing uses and the latest risk assessment indicates that most of the occupational scenarios do not result in risk concern, with the exception of inhalation risks to mixer/loaders for aerial application. PF5 respirators are required to alleviate risk concerns for this application scenario.

Timeline:
EPA has created the following estimated timeline for the completion of the fomesafen registration review.

Activities	Estimated Month/Year
Phase 1: Opening the docket	
Open Public Comment Period for Fomesafen Docket	Mar. 2007
Close Public Comment Period	June 2007
Phase 2: Case Development	
Develop Final Work Plan (FWP)	Aug. 2007
Open Public Comment Period for Preliminary Risk Assessments	Feb. 2010
Close Public Comment Period	Apr. 2010
Phase 3: Registration Review Decision	
Open Public Comment Period for Proposed Reg. Review Decision	Aug. 2010
Close Public Comment Period	Nov. 2010
Final Decision and Begin Post-Decision Follow-up	Mar. 2010
Total (years)	**3.0**

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 fomesafen 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 Limits (MRLs) or disparities between U.S. tolerances and MRLs in key export markets, providing as much specificity as possible regarding the nature of the concern.

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 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, 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
13. Fomesafen is not identified as a cause of impairment for any waterbodies listed as impaired under section 303(d) of the Clean Water Act, based on information provided at http://www.epa.gov/oppsrrd1/registration_review/water_quality.htm. However, the Agency invites submission of water quality data for this chemical. To the extent possible, data elements identified in Appendix A of the "OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process" should be provided, in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.
    See http://www.epa.gov/oppsrrd1/registration_review/water_quality.htm.

Next Steps:

After the comment period closes in July 2007, the Agency will prepare a Final Work Plan for this pesticide.

II. FACT SHEET

Background Information:

- Fomesafen registration review case number: 7211.
- Fomesafen PC Code: 123802, CAS#: 108731-70-0.
- Technical registrant: Syngenta Crop Protection, Inc., and BASF Corporation (multiple active ingredient products, also containing the sodium salt of bentazon).
- First approved for use in a registered product in 1980's for soybean.
- Approved for use on snap beans, dry beans, and cotton in 2006.
- No data call-in needed.
- The tolerances were reassessed during a 2006 registration action.
- Special Review and Reregistration Division Chemical Review Manager (CRM): Wilhelmena Livingston: livingston.wilhelmena@epa.gov.
- Registration Division Product Manager (PM): Joanne Miller: miller.joanne@epa.gov.

Use & Usage Information: (For additional details, please refer to the BEAD Appendix A document in the fomesafen docket.)

- Fomesafen is a pre-plant, pre-emergence and post-emergence herbicide used on soybeans, snap beans, dry beans, and cotton. It is also registered for use on agricultural fallow/idleland, nonagricultural uncultivated areas/soils, pine (forest/shelterbelt) and pine (seed orchard).
- There are no residential uses.
- Fomesafen can be applied through aerial and ground spray.
- Nearly 640,000 pounds of fomesafen are used annually with highest usage on soybeans, dry beans, and snap beans.
- Pests controlled include broadleaf weeds, grasses, and sedges.
- There are eight section 3 registrations, and 10 section 24(c) registrations (Special Local Need).

Recent Actions:

- A notice of a filing of a pesticide petition for the establishment of a regulation for the residues of sodium salt of fomesafen in or on dry and snap beans, and cotton seed and gin byproducts was issued on March 1, 2006. This request was submitted from IR-4 and Syngenta Crop Protection, Inc.
- A final rule for sodium salt of fomesafen was issued on May 3, 2006 (FR Vol. 71 No. 85) which established tolerances for residues of fomesafen in or on dry beans, snap beans and cotton.

Ecological Risk Assessment Status:

The following are key findings of the fomesafen risk assessment that was conducted to incorporate new uses of fomesafen. Please refer to Section III, Ecological Risk Assessment Problem Formulation, for a detailed discussion of the ecological risk assessment. A summary follows:

- The most recent environmental fate and ecological risk assessment was conducted on January 30, 2006 for new uses of fomesafen on dry beans, snap beans, and cotton. This assessment is also applicable to soybeans.
- Fomesafen is persistent and mobile in both water and soil.
- Fomesafen does exert toxic effects on aquatic plants but risk quotients for the scenarios modeled are below the level of concern (LOC).
- The greatest acute risk associated with fomesafen use is for non-target terrestrial plants.
- Fomesafen is non-toxic to slightly toxic to aquatic animals, both freshwater and estuarine/marine. No direct effects to aquatic animals are anticipated based on existing rates.
- Fomesafen is practically non-toxic to slightly toxic to birds and mammals on an acute basis. No acute risk LOCs were exceeded, but acute endangered species risk LOCs were exceeded for small mammals. There were chronic risks to birds and mammals at all application rates evaluated.
- Based on LOC exceedences and co-occurrence of species with crops (at the county level), 807 endangered species were identified as potentially being at risk for direct effects from fomesafen use. Of these, greater than 70% were plants.
- Spray drift management language as well as language to limit drift into sensitive areas (e.g. residential areas, bodies of water, non-target plant) is required on the labels.

Human Health Risk Assessment Status:

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

Fomesafen has low acute toxicity by the oral route of exposure. It is severely irritating to the eye and is a moderate skin irritant. In the subchronic and chronic feeding studies, the consistent finding is the effect in the liver characterized by increases in liver weight and in associated enzymes including alkaline phosphatase, alanine transaminase, and aspartate transaminase. Hyalinization of the liver is also observed.

Dietary (Food and Water):

- The most recent acute and chronic dietary assessments were conducted on 02/28/06 for a proposal to amend use on soybeans, and a proposal to add uses on cotton, snap beans, and dry beans.
- This 2006 assessment included an aggregate assessment that considered dietary exposure to fomesafen from both food and drinking water.
- There were no dietary risks that exceed the Agency's LOC.

Residential:

- There are no residential uses of fomesafen.

Occupational:

- An occupational assessment was conducted as a part of the 2006 risk assessment for all existing uses. The latest risk assessment indicated that most of the occupational scenarios did not result in risk of concern, with the exception of inhalation risks to mixer/loader for aerial application. PF5 respirators were required to preclude risks from this use scenario.

Tolerances:

Commodity	U.S. (ppm)	Codex (mg/kg)	Canada (ppm)
Soybean	0.050		0.05
Cotton, undelineated seed	0.025		
Cotton, gin byproducts	0.025		
Bean dry	0.025		0.05
Bean, snap, succulent	0.025		0.05
Lima beans			0.05

Data Call-In Status:

- A data call-in is not required.

Labels:

- A list of registration numbers may be found in the fomesafen 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

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

PC Code: 123802
DP Barcode: 306023

MEMORANDUM

Subject: EFED Problem Formulation for Fomesafen Registration Review

To: Wilhelmena Livingston, Chemical Review Manager
Special Review and Reregistration Division
U.S. EPA, Office of Pesticide Programs

From: Paige Doelling Brown, Ph.D., Fisheries Biologist
James Hetrick, Ph.D., Senior Chemist
Environmental Risk Branch 1
Environmental Fate and Effects Division (7507P)

Thru: Nancy Andrews, Branch Chief
Environmental Risk Branch 1
Environmental Fate and Effects Division (7507P)

Date: February 13, 2007

Attached please find EFED's problem formulation document in support of the Registration Review docket opening of fomesafen. This document supplants the previous registration review documents on fomesafen. This document is based on the January 30, 2006, EFED Ecological Risk Assessment (ERA) for new uses of fomesafen on cotton (DP 302766), snap beans (DP 314014), and dry beans (DP 314112). It outlines (1) the available environmental fate and effects studies, (2) the methods used in the ERA of fomesafen, (3) LOC exceedances, and (4) additional information needs.

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

REGISTRATION REVIEW

ECOLOGICAL RISK ASSESSMENT PROBLEM FORMULATION FOR:

FOMESAFEN

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STRESSOR SOURCE AND DISTRIBUTION

The source of the stressor considered in this document is sodium salt of fomesafen.

Fomesafen is an herbicide. It is applied as a foliar spray (both pre-emergent and post-emergent) for control of broad-leaved weeds, grasses, and sedges. Fomesafen is a diphenylether. It disrupts the cell membrane of the plant (www.syngentacroprotection-us.com) by penetrating into the cytoplasm and causing formation of peroxides and free electrons (www.abcbids.org). The specific mode of action is inhibition of protoporphyrinogen oxidase (www.weeds.iastate.edu). Fomesafen generally acts quickly, and does not translocate. It has both foliar and soil activity. Other herbicides in this group include aciflourfen, lactofen, and oxyfluorfen.

Fomesafen is highly persistent in soil (63-527 days, dependent on soil type) resulting in a potential for accumulation in terrestrial environments. The label suggests not planting sensitive crops in a fomesafen-treated field for a 3-18 month period, due to the persistence of fomesafen in the soil. Additionally, it is highly mobile, and is expected to leach into groundwater and be transported from the site via runoff into surface waters. Based on physical properties, bioaccumulation and long-range transport are not expected to be of concern. It is extremely toxic to terrestrial plants, especially dicots, but of fairly low acute toxicity to fish and wildlife. Some chronic reproductive effects have been noted in mammals, and may also occur in birds. No major degradates of toxicological concern have been identified.

INTEGRATION OF AVAILABLE INFORMATION

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

- Ecological Risk Assessment in Support of Docket Preparation for Registration Review of Fomesafen (DP 306023), January 18, 2006

ECOLOGICAL EFFECTS

AVAILABLE TOXICITY STUDIES

Toxicity endpoints are established based on data generated from guideline studies submitted by the registrant, and from open literature studies that meet the criteria for inclusion into the ECOTOX database maintained by EPA/ORD. EFED policy is to use the most sensitive endpoint for each taxa evaluated. In aquatic systems, taxa evaluated include aquatic plants, invertebrates, and fish. Fish serve as a surrogate for aquatic-phase amphibians. Where data are available, separate endpoints are used for freshwater and estuarine/marine organisms. In terrestrial systems, taxa evaluated include birds and mammals. Bird endpoints are generally derived from guideline studies on bobwhite quail

and/or mallard duck. Bird data is used as a surrogate for reptiles and terrestrial-phase amphibians. Mammal data is derived from guideline studies conducted on laboratory rats, mice, or rabbits.

Aquatic Guideline Data

Fomesafen was originally registered for use in the 1980s. Guideline studies from that time were available for aquatic invertebrates and fish, both freshwater and marine/estuarine. Although some of the studies were conducted on formulated product, and would not be acceptable under current standards, they were classified as core or supplemental under the guidelines at the time they were submitted. When necessary, endpoints were re-calculated and/or data were converted to express toxicity on the basis of active ingredient. Details of conversion are included in Appendix E. Aquatic plant data were submitted by the registrant (upon request by EFED), during the development of this risk assessment. Although the Data Evaluation Review (DER) process has not yet been completed for these studies, they have been provisionally classifed as Supplemental, and the toxicity data has been incorporated into the assessment. Overall, fomesafen is slightly toxic to practically nontoxic to invertebrates and practically non-toxic to fish on an acute basis (Table 1). Chronic data were also available, and are presented in Table 2.

Table 1 Acute Aquatic Data from Registrant-submitted Studies

Species	LC_{50} (ppm)	95% C.I. (ppm)	NOAEC (ppm)	Classification (MRID)
Freshwater Organisms				
Green alga[1] *(Selenastrum capricornutum)*	0.12 (biomass)	0.05-0.34	0.02	Supplemental (46673804) Technical
Water flea *(Daphnia magna)*	376 (practically nontoxic)	323-437	117	Core[2, 3] (163169) Formulation
Rainbow Trout *(Onchorynchus mykiss)*	126 (practically nontoxic)	117-135	80	Core[2, 3] (103023) Formulation
Estuarine/ Marine organisms				
Marine diatom[1] *(Skeletonema costatum)*	1.51 (biomass)	ND	0.94	Supplemental (46673806) Technical
Mysid shrimp *(Mysidopsis bahia)*	25 (slightly toxic)	19-38	ND	Core[2] (135647) Technical
Sheepshead minnow *(Cyprinodon varigetus)*	>163 (practically nontoxic)	ND	>163	Core[2, 3] (135651) Formulation

[1]Provisional data and classification, pending final review. [2]Data are from studies originally reviewed and classified in 1984, some of which used formulated product. [3]For purposes of this risk assessment, test concentrations were adjusted for percent a.i. if necessary, and endpoints were re-calculated using TOXANAL software. ND-not determined.

Table 2 Chronic Aquatic Data from Registrant-submitted Studies				
Species	***NOAEC (ppm)***	***LOAEC (ppm)***	**Endpoints Affected**	**Classification[1] (MRID)**
Freshwater Organisms				
Water flea *(Daphnia magna)*	50	100	Reduced growth, Total # of offspring	Core (135642) Formulation
Estuarine/ Marine organisms				
Mysid shrimp *(Mysidopsis bahia)*	0.7	1.7	Parental mortality	Core (135648) Formulation
Sheepshead minnow[2] *(Cyprinodon varigetus)*	12.2	20.1	Reduced larval survival	Core (135644) Formulation

[1]Data are from studies originally reviewed and classified in 1984, some of which used formulated product. [2]For purposes of this risk assessment, test concentrations were adjusted for percent a.i.

Aquatic Data from ECOTOX

The ECOTOX database was accessed, and no toxicity data for fomesafen were located.

Terrestrial Plant Guideline Data

Terrestrial plant guideline studies were submitted during the development of this risk assessment. Data are shown below (Table 3), but are considered provisional pending final data evaluation review. Fomesafen is effective, both pre- and post-emergent, against a variety of plants, although dicots appear to be more sensitive than monocots for both endpoints. The product is marketed as a control for broad-leafed weeds. In some cases, calculated EC_{25}s were below the concentrations tested, so a NOAEC was not determined. The most sensitive endpoint, used in the risk assessment, is the vegetative vigor EC_{25} for radish (0.0016 lb ai/A).

Table 3 Terrestrial Plant Guideline Data					
Species	***Common name***	***Class***	***EC_{25} (lb ai/A)***	**NOAEC (lb ai/A))**	**Classification[1] (MRID)**
Vegetative Vigor					
Raphanus sativus	Radish	D	0.0016	0.00098	Supplementary (46673802)
Echinochloa crus-galli	Barnyard grass	M	0.31	0.25	
Seedling emergence					

Lycopersicon esculentum	Tomato	D	0.005	ND	Supplementary (46673801)
Allium cepa	Onion	M	0.089	ND	

[1] Provisional classification, pending final data evaluation review.

Efficacy data (MRID 135656) were part of the data package submitted. The efficacy data included pre-emergence and post-emergence treatment of 24 plant species, at two concentrations (0.25 and 1.0 kg ai/ha). The two concentrations bracket the currently proposed rates (0.42 and 0.54 kg ai/ha). The plant species tested included both monocots (11 species) and dicots (13 species). Both crop (7 species) and non-crop (17 species) plants were evaluated. With the exception of soybeans, all plants tested experienced >20% "damage" when treated pre-emergence, with a significant number (65%) experiencing >80% damage when treated with the lower concentration (0.25 kg ai/ha). Applied post-emergence, fomesafen is slightly less effective, with "damage" typically in the 0-40% range for monocots and 40-80% range for dicots. The report did not specify how damage was quantified.

Avian and Small Mammal Guideline Data

Guideline studies were available for birds (both dose and dietary), and small laboratory mammals (dose). On the basis of both dose and dietary values, fomesafen is practically non-toxic to birds and slightly toxic to mammals (Table 4). Endpoints for female guinea pigs and mallard ducks were used to develop risk quotients.

Table 4 Avian and Small Mammal Guideline Data from Acute Studies

Species	LC_{50} (ppm)	95% C.I. (ppm)	NOAEC (ppm)	Classification[1] (MRID)
Acute dose				
Mallard duck	>5,000 (practically non-toxic)	ND	ND	Core (163168)
Rat	F 1499 M 1858 (slightly toxic)	(1302-1749) (1420-2546)	1219 975	Minimum (164901)
Mouse	F 745 M 766 (slightly toxic)	(512-1286) (525-1341)	487 312	Minimum (164901)
Guinea Pig	F 607 (slightly toxic)	ND	244	Minimum (164901)
Acute dietary				
Bobwhite quail	>20,000 (practically non-toxic)	ND	13,333	Core (103022)
Mallard duck	>20,000 (practically non-toxic)	ND	20,000	Core (163384)

[1] Data are from studies originally reviewed and classified in 1984.
ND-Not determined

Chronic guideline studies (Table 5) were available for birds (mallard duck and bobwhite quail) and small laboratory mammals (rat). Bird guideline studies did not establish a LOAEC, only determining that there were no effects at the highest (mean-measured) concentration tested. This contributes significant uncertainty to the evaluation of chronic risk to birds. The mallard duck NOAEC (46 ppm) is used in the determination of chronic risk to birds, but it may overestimate the risk to birds. In some cases, calculated exposure is near or above the maximum tested concentration.

Table 5 Avian and Small Mammal Guideline Data from Chronic Studies

Species	*NOAEC (ppm)*	*LOAEC (ppm)*	Endpoint Affected	Classification[1] (MRID)
Bobwhite quail	51	ND	None	Core (135640)
Mallard duck	46	ND	None	Core (135639)
Rat	250	1000	Number of pups born live, number of pups surviving	Acceptable (144862)

[1]Data are from studies originally reviewed and classified in 1984.
ND-Not determined

Terrestrial Insect Data

Guideline tests for honeybees were submitted (MRID 135651, Core), as was a field chronic effects study on earthworms (MRID 135652). The acute oral LD50 for honeybees was >50 µg ai/bee, and the acute contact LD_{50} was >100 µg ai/bee. The field test for earthworms included two applications of fomesafen, applied at one-year intervals. Fields were treated with 0.5 kg ai/ha and 5.0 kg ai/ha. No adverse effects on total numbers, total weights, or numbers of individual species were noted at the 0.5 kg ai/ha treatment level. A significant change in numbers of one species of earthworm *(Allolobophura nocturna)* was noted at the higher treatment level, but authors attributed this to modifications in grass cover caused by the herbicide treatment rather than direct toxic effects.

Studies were also submitted (MRID 135656) for eight species of invertebrates, from the orders Acarina, Hemiptera, Diptera, Lepidoptera, Coleoptera, and Nemotoda. Fomsafen was applied to multiple life stages at concentrations of 250 and 500 ppm. The greatest level of mortality in these tests was 9%. Aphids *(Aphis fabae)* experienced mortality rates of 9% at concentrations of 250 ppm and 500 ppm.

Terrestrial Data from ECOTOX

The ECOTOX database was accessed, and no toxicity data for fomesafen were located

Incident Reports

EFED maintains EIIS, a database containing reported incidents of damage to non-target species caused by pesticide use. There are a total of 28 reported incidents for fomesafen, 27 of which are damage to agricultural crops. Incidents reported cover a range of 9 years (1994-2002), but many of them (54%) were reported in 2002. Corn was the crop most frequently reported damaged, accounting for 21 out of the 24 cases for which the specific crop was reported. In some cases (5) the fomesafen was applied directly to the damaged crop, and the legality was classified as misuse or accidental misuse. In other cases (17) the damaged was caused by drift, legality of application unknown. The certainty that the incident was related to fomesafen use was generally classified as probable. Other crops damaged included green peas, cotton, and soybeans under registered use conditions.

There is one report of a fish kill. In this incident, there was a report of approximately 200 fish (channel catfish, crappie, largemouth bass, and redear sunfish) dying following a legal application to a soybean site. The certainty of the kill being related to fomesafen runoff is classified as possible. Application was in accordance with registered use.

EXPOSURE CHARACTERISTICS

Major routes of fomesafen dissipation are leaching, runoff, and microbial degradation. Because fomesafen is persistent and mobile in soil, it is expected to move from the application site into groundwater and surface water. Additionally, off-site movement of fomesafen is expected through spray drift from aerial and ground spray. The high persistence of fomesafen is expected to contribute to year-to-year accumulation in terrestrial and aquatic environments.

Fomesafen is stable to abiotic hydrolysis. It undergos slow photodegradation in water ($t_{1/2}$= 49 to 289 days). Fomesafen is persistent ($t_{1/2}$=9 to 99 weeks) in aerobic soil and aquatic environments. However, it degrades rapidly ($t_{1/2}$< 20 days) in anaerobic environments. The major degradation product of fomesafen is 5-(2-chloro-α,α,α-trifluoro-p-tolyloxy)-N-methylsulphonyl-panthranilamide (fomesafen amine). A minor degradation product is 5-(2-chloro-α,α,α-trifluoro-p-tolyloxy) anthranilic acid (fomesafen amino acid). Neither degradate has been identified as a toxicological concern.

Fomesafen is expected to be very mobile in soil. Simple partitioning coefficients range from 0.51 in loamy coarse sand to 2.45 in sandy clay loam soil. Regression analysis indicates fomesafen sorption is not dependent on soil organic matter content. Aged soil column leaching studies indicate degradation products of fomesafen are not mobile in soils; less than 0.06% of applied radioactivity was detected in the leachate samples.

Field dissipation studies in NC, IL, MS, AR, AL, TX, LA, SD, MN, KY, IA and MO indicate fomesafen is moderately persistent to persistent ($t_{1/2}$= 50 to 150 days) in surface soils under actual use conditions. Fomesafen was detected at depths up to 30 inches in

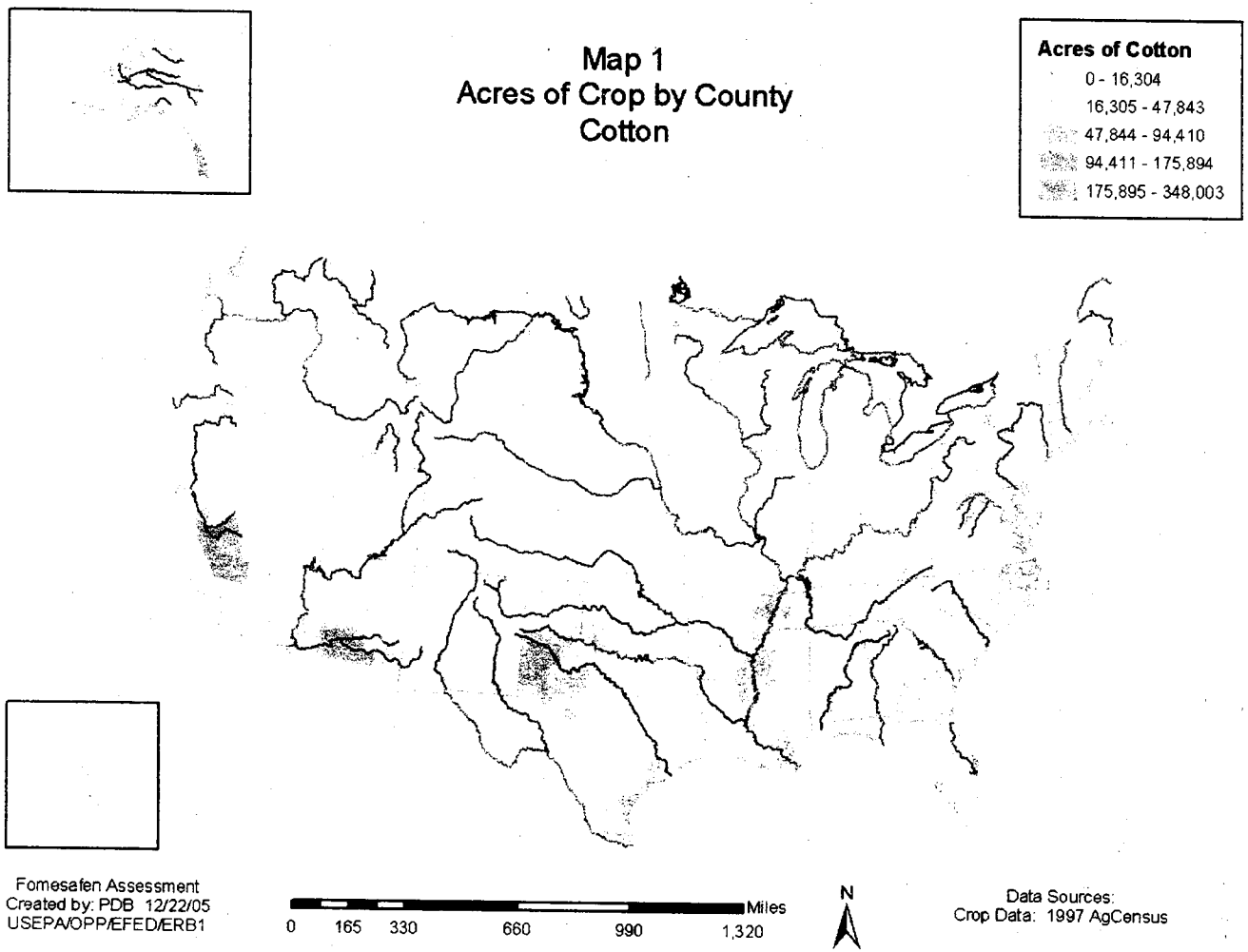
the soil profile. Fomesafen amine was the only degradation product identified in field dissipation studies. Prospective ground water monitoring in NC indicates fomesafen moved through the soil profile into medium and deep ground water.

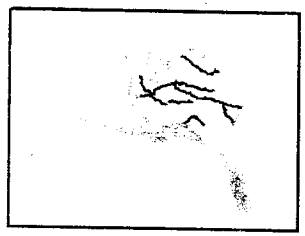
Fomesafen has a low potential for bioaccumulation in fish tissues. Bioaccumulation factors for fosmesafen were 0.7 for whole fish, 0.2 for edible tissues, and 5.2 for nonedible tissue. Bioaccumulated residues were depurated during a 14-day depuration period.

CHARACTERISTICS OF ECOSYSTEMS POTENTIALLY AT RISK

For typical crop applications, the ecosystem at risk is the field itself, in terms of organisms that might be sprayed during application, organisms affected by accumulation of fomesafen in the soil; and the adjacent aquatic and terrestrial environments affected due to runoff, spray drift, or groundwater contamination. In water bodies receiving runoff from agricultural fields, pelagic and benthic elements are considered. Terrestrial organisms assessed include non-target plants, insects, amphibians, reptiles, birds, and mammals. Because fomesafen is an herbicide, potential affects on non-target plants have been addressed at length.

Fomesafen is being proposed as a pre-plant, pre-emergence, and post-emergence herbicide for use on broadleaf weeds, grasses, and sedges, in snap beans, dry beans, and cotton. Methods of application are ground spray (0.5 lb ai/A, cotton) and aerial spray (0.375 lb ai/A, dry beans, snap beans, and cotton). Application is limited to once a year, or in alternate years, depending on location. Application rates are regionally specific. Maps 1, 2, and 3 show the locations of these crops according to USDA crop data.

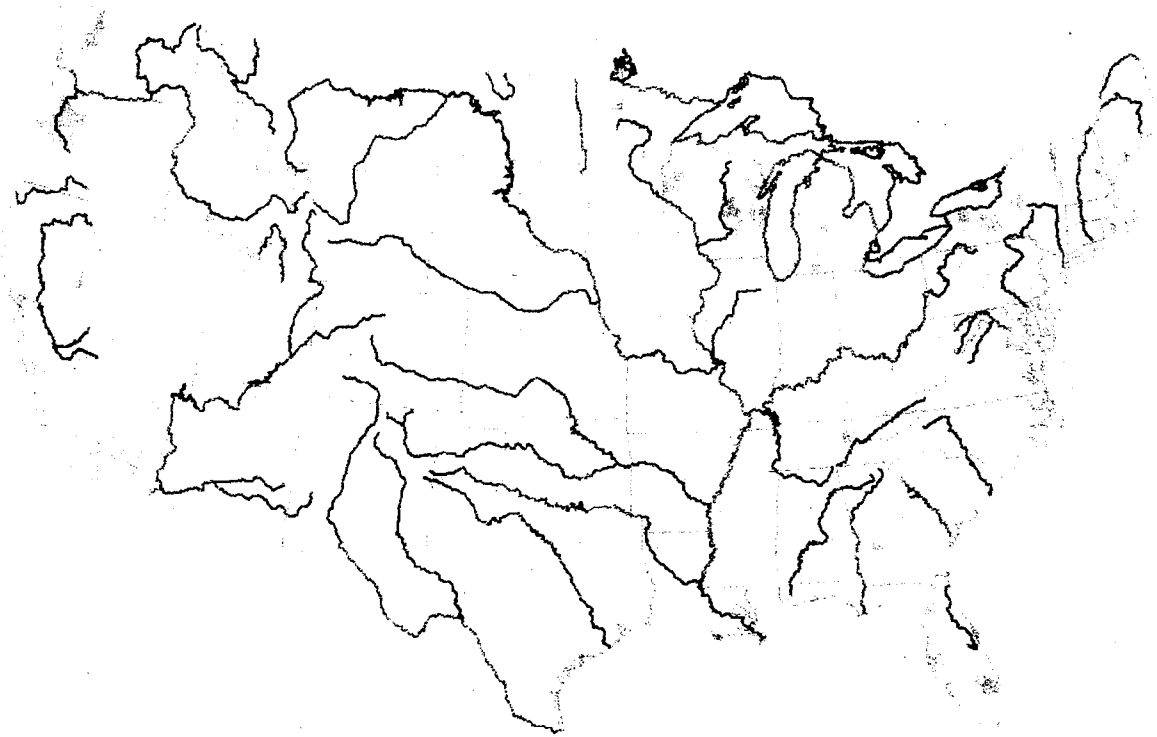

Map 1
Acres of Crop by County
Cotton
Acres of Cotton
0 - 16,304
16,305 - 47,843
47,844 - 94,410
94,411 - 175,894
175,895 - 348,003
Fomesafen Assessment
Created by: PDB 12/22/05
USEPA/OPP/EFED/ERB1
0 165 330 660 990 1,320
Miles
N
Data Sources:
Crop Data: 1997 AgCensus

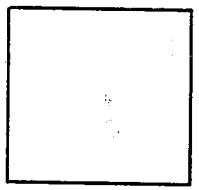


Map 2
Acres of Crop by County
Snap Beans

Acres of Snap Beans

- 0 - 467
- 468 - 1,654
- 1,655 - 3,933
- 3,934 - 7,403
- 7,404 - 13,690



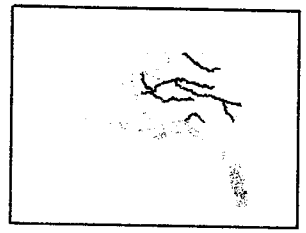


Fomesafen Assessment
Created by: PDB 12/22/05
USEPA/OPP/EFED/ERB1

0 165 330 660 990 1,320 Miles

N

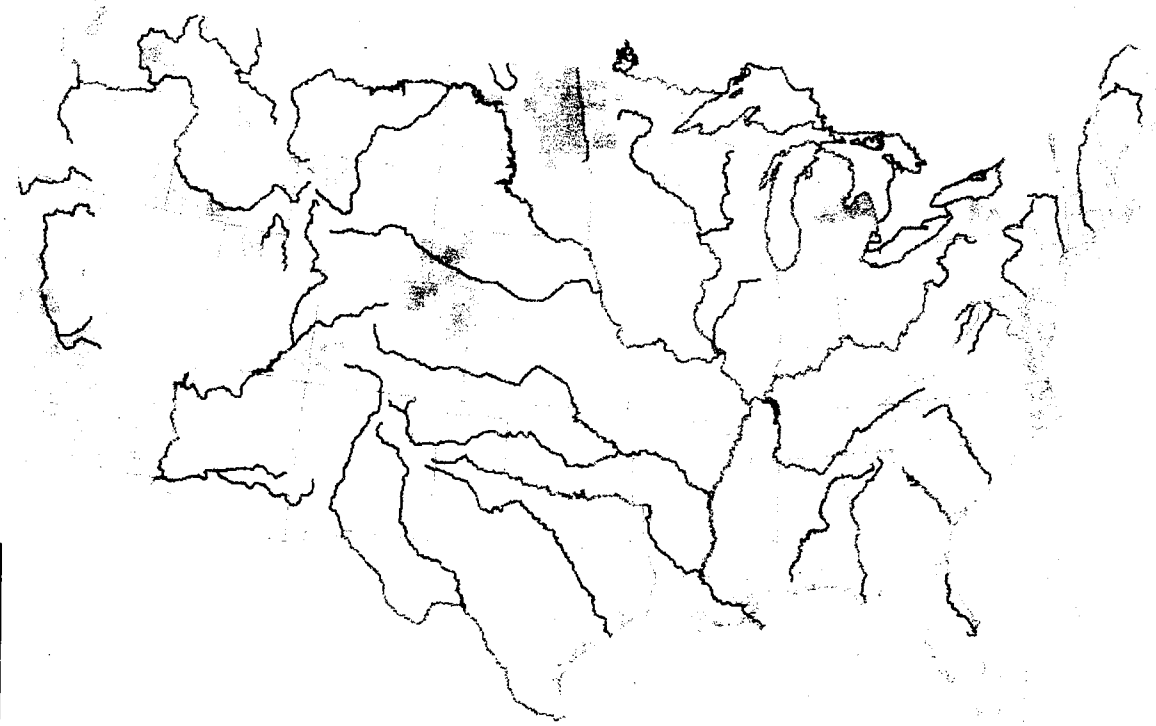
Data Sources:
Crop Data: 1997 AgCensus

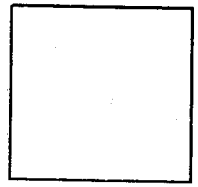


Map 3
Acres of Crop by County
Dry Beans, including Dry Limas

Acres of Dry Beans

- 0 - 2,470
- 2,471 - 7,414
- 7,415 - 15,606
- 15,607 - 39,664
- 39,665 - 103,604





Fomesafen Assessment
Created by: PDB 12/22/05
USEPA/OPP/EFED/ERB1

0 155 310 620 930 1,240 Miles

N

Data Sources:
Crop Data: 1997 AgCensus

ASSESSMENT ENDPOINTS

Assessment endpoints are defined as "explicit expressions of the actual environmental value that is to be protected." Defining an assessment endpoint involves two steps: 1) identifying the valued attributes of the environment that are considered to be at risk; and 2) operationally defining the assessment endpoint in terms of an ecological entity (i.e., a community of fish and aquatic invertebrates) and its attributes (i.e., survival and reproduction). Therefore, selection of the assessment endpoints is based on valued entities (i.e., ecological receptors), the ecosystems potentially at risk, the migration pathways of pesticides, and the routes by which ecological receptors are exposed to pesticide-related contamination. The selection of clearly defined assessment endpoints is important because they provide direction and boundaries in the risk assessment for addressing risk management issues of concern. Changes to assessment endpoints are typically estimated from the available toxicity studies, which are used as the measures of effects to characterize potential ecological risks associated with exposure to a pesticide, such as paclobutrazol.

To estimate exposure concentrations, the ecological risk assessment considers a single application at the maximum application rate to fields that have vulnerable soils. The most sensitive toxicity endpoints are used from surrogate test species to estimate treatment-related direct effects on acute mortality and chronic reproductive, growth and survival assessment endpoints. Toxicity tests are intended to determine effects of pesticide exposure on birds, mammals, fish, terrestrial and aquatic invertebrates, and plants. These tests include short-term acute, sub-acute, and reproduction studies and are typically arranged in a hierarchical or tiered system that progresses from basic laboratory tests to applied field studies. The toxicity studies are used to evaluate the potential of a pesticide to cause adverse effects, to determine whether further testing is required, and to determine the need for precautionary label statements to minimize the potential adverse effects to non-target animals and plants.

Evaluation of ecological effects focuses initially on direct effects to the groups of organisms residing in the ecosystems at risk, based on ratios of the estimated environmental concentration (EEC) to a designated toxicity endpoint for a surrogate test organism. If pre-established levels of concern (LOCs) are exceeded for direct effects, indirect effects to endangered species (*e.g.* food chain, decrease in community diversity) are evaluated based on the group of organisms exceeding the LOC.

Direct

Direct effects evaluated are the survival, growth, and reproduction of various taxa of organisms potentially exposed to fomesafen. Taxonomic groups evaluated include aquatic plants (algae and vascular), aquatic invertebrates, aquatic vertebrates, terrestrial plants, terrestrial invertebrates, birds, and mammals. Both acute and chronic effects are considered.

Indirect

When herbicides are applied, indirect effects may include a decline in primary productivity, or change in composition of plant communities proximate to the treated area

or systems (wetlands and water bodies) receiving runoff from the site. If LOCs are exceeded for any taxa, potential indirect effects to endangered species are assessed.

CONCEPTUAL MODEL

In order for a chemical to pose an ecological risk, it must reach ecological receptors in biologically significant concentrations. An exposure pathway is the means by which a pesticide moves in the environment from a source to an ecological receptor. For an ecological exposure pathway to be complete, it must have a source, a release mechanism, an environmental transport medium, a point of exposure for ecological receptors, and a feasible route of exposure. The conceptual model (**Figure 1**) depicts the potential pathways for ecological risk associated with fomesafen use. The conceptual model provides an overview of the expected exposure routes for organisms within the fomesafen action area.

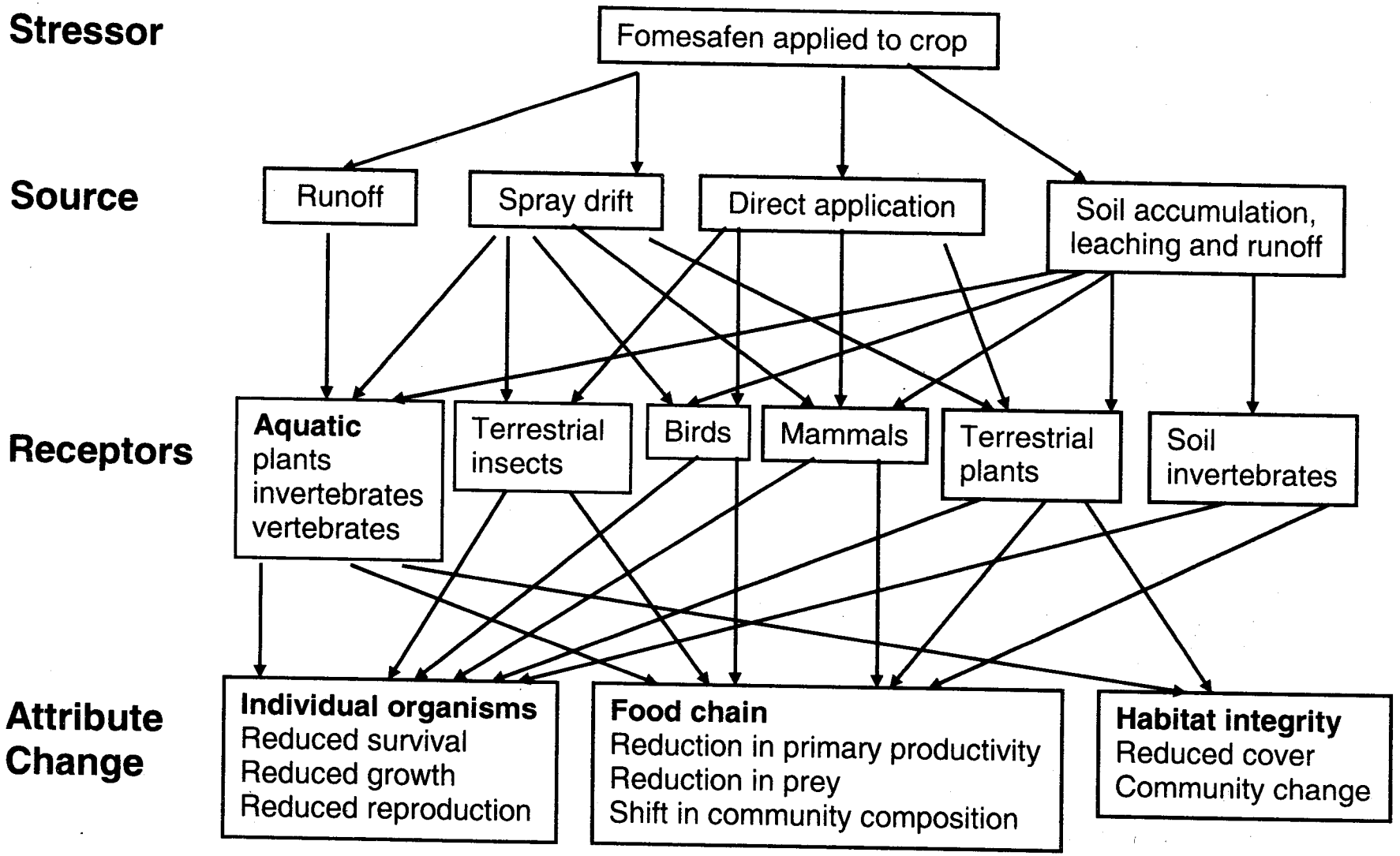


Figure 1 - Conceptual Model for Fomesafen

- Fomesafen deposited on plant surfaces may affect growth, survival, or fecundity of birds and/or small mammals ingesting the affected vegetation.
- Fomesafen accumulating in soil may be toxic to non-target plants.
- Fomesafen in runoff from treated areas may kill aquatic plants, aquatic invertebrates, or fish.
- Fomesafen in runoff from treated areas may reduce populations of aquatic plants, aquatic invertebrates, or fish, causing changes in the community.
- Fomesafen in runoff from treated areas may accumulate in sediments, resulting in chronic impacts to the benthic community.
- Fomesafen is expected to move from the application site by leaching into groundwater and runoff into surface water. Use of water resources with fomesafen occurrence as an irrigation source water may adversely impact non- target plants.

ANALYSIS PLAN OPTIONS

The registration review screening level risk assessment is based on an overview document compliant risk assessment for fomesafen use on cotton, dry beans, and snap beans (Ecological Risk Assessment in Support of Docket Preparation for Registration Review of Fomesafen (DP 306023), January 18, 2006. .

MEASURES OF EXPOSURE

AQUATIC EXPOSURE

Tier II EFED aquatic exposure models use the linked Pesticide Root Zone Model and Exposure Analysis Model System (PRZM-EXAMS). PRZM uses the chemical's physical and environmental fate properties and the site characteristics to predict the concentration of pesticide in runoff and entrained sediment from the field. EXAMS estimates the concentration of pesticide in an edge-of-field small water-body receiving runoff from the field. The water-body has no outflow with a constant volume (20 million liters), and is intended to represent an upper-end occurrence concentration.

PRZM-EXAMS Modeling for Surface Water

The aquatic exposure assessment for fomesafen was conducted to assess use on soybeans and cotton. Soybeans were used a surrogate for dry beans and snap beans, as EFED currently has no standard scenarios for these crops. Standard scenarios were selected to assess runoff potential from vulnerable use sites in MS (soybean and cotton), NC (cotton), and TX (cotton). Input

parameters for fomesafen were selected according to EFED Input Parameter Guidance for PRZM/EXAMS[1]. Input parameters are shown in Table 6.

Table 6 Input Parameters for PRZM-EXAMS Modeling of Fomesafen on Cotton and Soybeans

Parameter	Value	Comments	Source
Application Rate (kg a.i./ha)- Cotton	0.42	Aerial Spray	Label[1]
Application Rate (kg a.i./ha)- Cotton	0.56	Ground Spray	Label[1]
Application Rate (kg a.i/ha)- Soybean	0.42	Aerial Spray	Label[1]
Molecular Weight (grams/mole)	420		EPA 2020220
Solubility (mg/L)	1200	@pH= 7; 20^{0}c	MRID 45048207
Vapor Pressure (torr)	<7.5x10^{-7}	@ 50°C	HSDB
Henry's Constant (atm m^3/mol)	7.5 x10^{-13}	Estimated	HSDB
Kd (L/kg)	0.68	Lowest non-sand K_d	Acc No. 259413
Aerobic Soil Metabolism Half-life (days)	428.8	Upper 90th percentile of mean[2]	Acc No. 071059 Acc. No. 00135660
Aerobic Aquatic Metabolism Half-life (days)	115.7	Upper 90th percentile of mean[3]	Acc. No. 72158
Anaerobic Aquatic Metabolism Half-life (days)	Stable	Conservative Assumption	No Data Available
Photodegradation in Water (days)	289	@pH=7	MRID 40451101
Hydrolysis Half-life (days)	Stable	@pH=7	Acc No. 071059

1-Reflect application rates on the REFLEX 2LC, REFLEX 2.5 and REFLEX labels
2-Calculated from half-lives of 187.6, 630, 57, 693, 349.3, 527.1, 207 days using a mean of 387.84 days and standard deviation of 242.90 days.
3- Calculated from half-lives of 139.9, 60.9, 92.4, and 115.5 days using a mean of 102 days and standard deviation of 33.44 days.

For aerial applications (Table 7), peak 1 in 10 year estimated environmental concentrations (EECs) ranged from 7.5 ppb (soybeans, MS) to 12.2 ppb (cotton, TX). Chronic 1-in-10 year (21-day average and 60-day average) EECs ranged from 6.4 ppb (soybean, MS, 60-day average) to 11.4 ppb (cotton, MS &TX, 21-day average).

Table 7 PRZM-EXAMS EECs for Fomesafen at 0.375 lb a.i/A[1]

Region	Crop	State	Peak	4 days	21 days	60 days
			µg/L (ppb)			
1	Soybean	MS	7.462	7.382	7.133	6.443
1	Cotton	MS	12.102	11.964	11.411	10.115
1	Cotton	NC	9.856	9.728	9.201	8.067
1	Cotton	TX	12.201	12.045	11.437	9.973

1-Concentrations were derived for 0.375 lb ai/A using aerial applications

Peak 1-in-10 year EECs for ground spray applications (Table 8) ranged from 10.6 ppb (cotton, NC) to 15.1 ppb (cotton, MS). Chronic 1 in 10 year (21-day average and 60-day average) concentrations ranged from 8.6 ppb (cotton, MS, 60-day average) to 14.2 ppb (cotton, MS, 21-day average).

[1] **Guidance for Selecting Input Parameters in Modeling the Environmental Fate and Transport of Pesticides. Version II, 2/28/02.**

Table 8 PRZM-EXAMS EECs for Fomesafen at 0.50 lb ai/A						
Region	Crop	State	Peak	4 days	21 days	60 days
			µg/L			
1	Cotton	MS	15.106	14.939	14.249	12.621
1	Cotton	NC	10.609	10.471	9.905	8.680
1	Cotton	TX	14.63	14.445	13.713	11.954

1- Concentrations were derived for 0.50 lb ai/A using ground spray

SCIGROW Modeling for Ground Water

Because fomesafen is mobile and persistent in soil, a screening level groundwater assessment using SCIGROW (ver. 2.3) was conducted to estimate the concentration of fomesafen in shallow groundwater, which could potentially be used for crop irrigation. Input parameters for SCIGROW are listed in Table 9. A groundwater monitoring study was submitted (MRID 42247001), but the shallow groundwater wells were dry during the study. Fomesafen was detected in soil porewater at concentrations of 1 µg/L (at 4 months), up to 17 µg/L (at 1 month). It was detected at a concentration of 1 µg/L in the medium- to deep-depth wells.

Table 9 Input Parameters for SCIGROW Modeling for Fomesafen			
Parameter	Value	Comments	Source
Application Rate (kg a.i./ha)- Cotton	0.56		Label[1]
K_{oc} (L/kg)	68	Estimated[2]	Acc No. 259413
Aerobic Soil Metabolism Half-life (days)	387.84	Mean[3]	Acc No. 071059 Acc. No. 00135660

1-Reflect maximum application rates on the REFLEX 2LC, REFLEX 2.5 and REFLEX labels
2-Koc estimated using Kd/SOC=Koc; where Kd=0.68 and SOC=1% SOC percentage
3-Calculated from half-lives of 187.6, 630, 57, 693, 349.3, 527.1, 207 days using a mean of 387.84 days and standard deviation of 242.90 days.

Based on the SCIGROW estimate, the concentration of fomesafen in shallow ground water in sand soils is not expected to exceed 6.68 µg/L. A groundwater monitoring study was submitted (MRID 42247001), but the shallow groundwater wells were dry during the study. Fomesafen was detected in soil porewater at concentrations of 1 µg/L (at 4 months), up to 17 µg/L (at 1 month). It was detected at a concentration of 1 µg/L in the medium- to deep-depth wells.

Because fomesafen is expected to leach to groundwater, EFED has calculated the maximum application rate of fomesafen from two inches of irrigation water, using the following equations. This calculation assumes that two inches (0.167 ft) of irrigation water is required for optimum plant growth. The calculations are as follows:

43,560 ft^2/A* 0.167 ft irrigation water= 7,274 ft^3 for 2 inches of irrigation water/A

7,274 ft^3 irrigation water/A* 28.316846 liter/ft^3=205,991.13 liters of irrigation water/A

205,991.13 liter of irrigation water/A *EEC :g/L = fomesafen :g/A

(fomesafen :g/A)/ (10^6) = fomesafen grams/A*1lb/454 grams=fomesafen lbs ai/A.

Based on two inches of irrigation and the SCIGROW estimate, the application rate of fomesafen is estimated at 0.003 lbs ai/A. Using the concentrations of 1 mg/L and 17mg/L (from the groundwater study) as outer bounds, concentrations of fomesafen in irrigation water could range from 0.0004-0.0077 lbs ai/A.

Soil Accumulation

Because of the persistence of fomesafen in soil, a screening level assessment was conducted to quantify the accumulation of fomesafen residues in soil. A first-order decay model ($A=A_0e^{-kt}$) was used to estimate fomesafen soil concentrations. The time period in the model (t) was set to 730 days to represent alternate years applications. The upper 90th percentile of the mean half-life ($t_{1/2}$=428 days; k=0.00161950 days^{-1}) was used to represent the microbial mediated decay rate of fomesafen in soil. The starting concentration (A_0) was set at the label recommended application rate of 0.375 lbs ai/A for aerial applications and 0.5 lbs ai/A for ground applications. The modeling scenario assumes that 100% of fomesafen residue is applied to the soil as recommended for a pre-emergent application. The model scenario also assumes that microbial degradation is the only route of dissipation from the application site. These assumptions are expected to exaggerate predicted formesafen soil concentrations.

Figure 2 illustrates the fomesafen concentrations in soil reach a plateau after approximately 10 years regardless of the application rate. Application rates of 0.375 lbs/A can theoretically result in a maximum fomesafen concentration of 0.14 mg/kg. Higher application rates of 0.5 lbs ai/A can theoretically result in a maximum fomesafen concentration of 0.19 mg/kg.

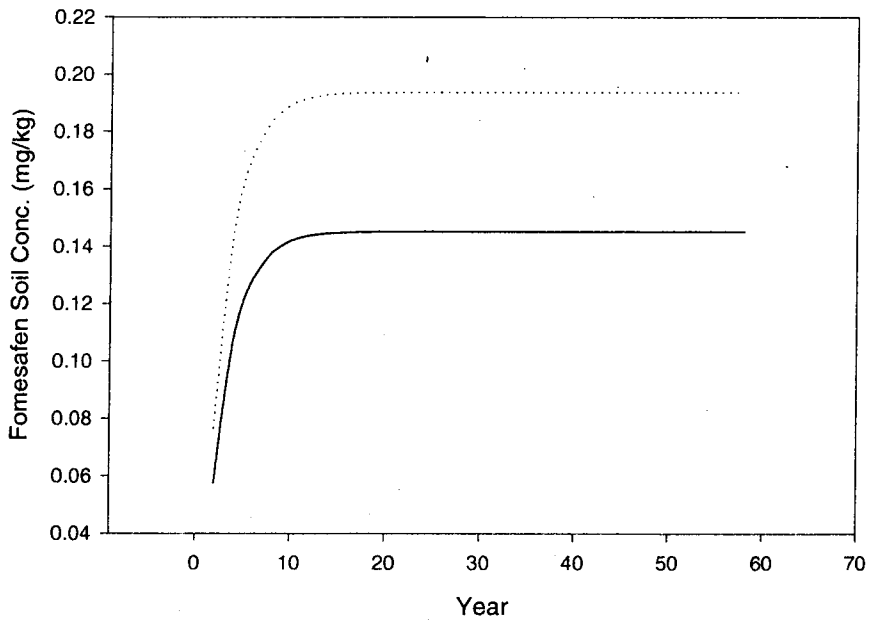


Figure 2 - Estimate of Fomesafen Loading in the Surface Soil (0-15 cm depth) from alternate year applications of 0.375 lbs/A (solid line) and 0.5 lbs/A (dotted line)

TERRESTRIAL EXPOSURE

AVIAN

For birds, dose estimates for the 0.2 lb ai/A application rate range from 0.87 mg/kg bwt (1000g frugivores, granivores, and insectivores) to 54.7 mg/kg bwt (20 g herbivores) (Table 10). At the 0.37 lb ai/A application rate, estimated doses range from 1.64 (1000g frugivores, granivores, and insectivores) to 102 (1000g fruit and pods). Dose estimates for the 0.49 lb ai/A application rate range from 2.14 mg/kg bwt (1000g frugivores, granivores, and insectivores) to 134 mg/kg bwt (20 g herbivores).

Table 10 Bird Dose Estimates

Feeding Categories	Kenaga Upper Bound Dose (mg/kg bwt)		
	Small (20 g)	Medium (100 g)	Large (1000 g)
0.2 lb ai/A Appllication Rate (Alternative)			
Short grass	54.67	31.17	13.96
Tall grass	25.06	14.29	6.40
Broadleaf plants/small insects	30.75	17.54	7.85
Fruits/pods/seeds/large insects	3.42	1.95	0.87
0.375 lb ai/A Application Rate			
Short grass	102.5	58.45	26.17
Tall grass	46.98	26.79	11.99
Broadleaf plants/small insects	57.66	32.88	14.72
Fruits/pods/seeds/large insects	6.41	3.65	1.64
0.50 lb ai/A Application Rate			
Short grass	133.93	76.38	34.19
Tall grass	61.39	35.01	15.67
Broadleaf plants/small insects	75.34	42.96	19.23
Fruits/pods/seeds/large insects	8.37	4.77	2.14

Small Mammals

For mammals dose estimates for the 0.2 lb ai/A application rate range from 0.10 mg/kg bwt (1000g granivore) to 45.8 mg/kg bwt (20 g short grass) (Table 11). At the 0.37 lb ai/A application rate, estimated doses range from 0.19 (1000g granivore) to 85.8 (20 g short grass). Dose estimates for the 0.49 lb ai/A application rate range from 0.25 mg/kg bwt (1000g granivore) to 112 mg/kg bwt (20 g short grass).

Table 11 Mammal Dose Estimates

Feeding Categories	Kenaga Upper Bound Dose (mg/kg bwt)		
	Small (15 g)	Medium (35 g)	Large (1000 g)
0.2 lb ai/A Appllication Rate (Alternative)			
Herbivores/Insectivores			
Short grass	45.76	31.63	7.33
Tall grass	20.98	14.50	3.36
Broadleaf plants/small insects	25.74	17.79	4.13
Fruits/pods/seeds/large insects	2.86	1.98	0.46
Granivores			
Fruits/pods/seeds/large insects	0.64	0.44	0.10
0.375 lb ai/A Application Rate			
Herbivores/Insectivores			
Short grass	85.81	59.30	13.75
Tall grass	39.33	27.18	6.30
Broadleaf plants/small insects	48.27	33.36	7.73
Fruits/pods/seeds/large insects	5.36	3.71	0.86
Granivores			
Fruits/pods/seeds/large insects	1.19	0.82	0.19
0.50 lb ai/A Application Rate			
Herbivores/Insectivores			
Short grass	112.12	77.49	17.97
Tall grass	51.39	35.52	8.23
Broadleaf plants/small insects	63.07	43.59	10.11
Fruits/pods/seeds/large insects	7.01	4.84	1.12
Granivores			
Fruits/pods/seeds/large insects	1.56	1.08	0.25

Plants

TerrPlant has two basic exposure scenarios. The first is an adjacent upland area, which is exposed to the pesticide via drift and dissolved concentrations in sheet runoff. The second is an adjacent semi-aquatic (wetland) area, which is exposed to the pesticide via drift and to dissolved concentrations in channelized runoff. Drift is calculated as a percentage of the application rate (1% for ground, and 5% for aerial, airblast, or spray chemigation) and is not adjusted for distance from the application site. The amount of dissolved pesticide in the runoff component is estimated based on solubility of the active ingredient. TerrPlant estimates are shown in Table 12.

Table 12 Terrestrial Plant Exposure

Application Method	Total Loading (Runoff +Drift) (lb ai/A)		Drift EEC (lb ai/A)
	Upland areas	Wetland areas	All areas
Use at 0.375 lb ai/A			
Aerial	0.0263	0.0938	0.0188
Ground	0.0113	0.0788	0.0038
Use at 0.50 lb ai/A			
Aerial	0.0343	0.1225	0.0245
Ground	0.0147	0.1029	0.0049

SUMMARY OF RISKS

AQUATIC RISKS

Fomesafen appears to be of relatively low toxicity to aquatic organisms, both animals and plants in freshwater and estuarine/marine systems (Table 13). Both acute and chronic effects were considered. Fomesafen may indirectly affect aquatic systems by damaging plants in adjacent wetland or riparian zones Modification of the vegetation in wetlands or riparian zones could cause decreased allochthonous input, increased sediment input, destabilization of the stream bank, or changes in the structural components (plant). Effects on waterbody-associated plant communities can be minimized by ensuring an adequate offset distance is maintained between the application site and the wetland or riparian zone. Appropriate distance is dependent on application rate, application methods, and weather conditions.

Table 13 Summary of Aquatic RQs			
Taxa	***Acute RQ***	**Chronic RQ[1]**	**Endangered Species RQ[2]**
Use on Beans at 0.375 lb a.i./A (MS scenario, aerial application)			
FW Aquatic Plants	0.06	NA[1]	0.33
FW Aquatic Invertebrates	<0.001	<0.001	<0.001
Fish	<0.001	NC	<0.001
SW Aquatic Plants	0.01	NA[1]	0.008
SW Aquatic Invertebrates	<0.001	0.01	<0.001
SW Fish	<0.001	<0.001	<0.001
Use on Cotton at 0.375 lb a.i./A (MS scenario, aerial application)			
FW Aquatic Plants	0.10	NA[1]	0.53
FW Aquatic Invertebrates	<0.001	<0.001	<0.001
FW Fish	<0.001	NC	<0.001
SW Aquatic Plants	0.01	NA[1]	0.013
SW Aquatic Invertebrates	<0.001	0.02	<0.001
SW Fish	<0.001	<0.001	<0.001
Use on Cotton at 0.5 lb a.i./A (MS scenario, ground application)			
FW Aquatic Plants	0.13	NA[1]	0.66
FW Aquatic Invertebrates	<0.001	<0.001	<0.001
FW Fish	<0.001	NC	<0.001
SW Aquatic Plants	0.01	NA[1]	0.016
SW Aquatic Invertebrates	<0.001	0.02	<0.001
SW Fish	<0.001	0.001	<0.001

[1] There are no chronic aquatic plants tests. [2] Endangered species RQ for plants are calculated based on NOAEC. Endangered species RQ for animals are calculated in the same way as acute risk values, but compared to a different LOC. NA – not applicable, NC – Not calculated, data not available.

TERRESTRIAL RISKS

AVIAN

At the proposed application rate of 0.5 lb ai/A, no acute dose- or dietary-based LOCs are exceeded for birds (Table 14). Chronic LOCs for birds in three out of the four food categories (short grass, tall grass, and broadleaf plants/small insects) are exceeded.

Table 14 Avian RQ Summary 0.5 lb ai/A					
Risk quotients based on Kenaga upper bound EECs	***Acute dose-based RQs***			***Acute dietary-based RQs***	**Chronic RQs**
	20g	***100g***	***1000g***	***All birds***	**All birds**
Short grass	0.05	0.02	0.01	0.01	2.56[c]
Tall grass	0.02	0.01	0.00	0.00	1.17[c]
Broadleaf plants/small insects	0.03	0.01	0.00	0.00	1.44[c]
Fruits/pods/seeds/lg insects	0.00	0.00	0.00	0.00	0.16[c]

[a] exceeds acute risk LOC (0.5)
[b] exceeds endangered species acute risk LOC (0.1)
[c] exceeds chronic risk LOC (1.0)

At the proposed application rate of 0.375 lb ai/A, no acute dose- or dietary-based RQs exceed any LOCs (Table 15). The chronic LOC is exceeded for birds consuming the food categories of short grass and broadleaf plants/small insects.

Table 15 Avian RQ Summary: 0.375 lb ai/A

Risk quotients based on Kenaga upper bound EECs	*Acute dose-based RQs*			*Acute dietary-based RQs*	Chronic RQs
	20g	*100g*	*1000g*	*All birds*	All birds
Short grass	0.04	0.02	0.01	0.00	1.96 [c]
Tall grass	0.02	0.01	0.00	0.00	0.90
Broadleaf plants/small insects	0.02	0.01	0.00	0.00	1.10 [c]
Fruits/pods/seeds/lg insects	0.00	0.00	0.00	0.00	0.12

[a] exceeds acute risk LOC (0.5)
[b] exceeds endangered species acute risk LOC (0.1)
[c] exceeds chronic risk LOC (1.0)

SMALL MAMMALS

At the proposed application rate of 0.50 lb ai/A, dose-based RQs exceed the endangered species LOC for two size classes of mammals (15g and 35 g) consuming short grass (Table 16). Using the dose-based RQ, chronic LOC is exceeded for mammals consuming the food categories of short grass (all weights), tall grass (15g, 35g), and broadleaf plants/small insects (15g, 35g). No chronic dietary based-RQs exceed any LOCs.

Table 16 Small Mammal RQ Summary: 0.50 lb ai/A

Risk Quotients based on Kenaga upper bound EEC	*Acute dose-based RQs*			Chronic dose-based RQs			Chronic dietary-based RQs
	15 g	*35 g*	*1000 g*	*15 g*	35 g	1000 g	All mammals
Short grass	0.13 [b]	0.11 [b]	0.06	4.08 [c]	3.49 [c]	1.87 [c]	0.47
Tall grass	0.06	0.05	0.03	1.87 [c]	1.60 [c]	0.86	0.22
Broadleaf plants/ small insects	0.07	0.06	0.03	2.30 [c]	1.96 [c]	1.05 [c]	0.26
Fruits/pods/seeds/ lg insects	0.01	0.01	0.00	0.26	0.22	0.12	0.03
Seeds (granivores)	0.00	0.00	0.00	0.06	0.05	0.03	NA

[a] exceeds acute risk LOC (0.5)
[b] exceeds endangered species acute risk LOC (0.1)
[c] exceeds chronic risk LOC (1.0)

At the proposed application rate of 0.375 lb ai/A, no acute dose-based RQs for mammals exceed any LOCs, although the RQ for small (15g) mammals consuming short grass equals the endangered species LOC (Table 17). Using the dose-based RQ, the chronic LOC is exceeded for

mammals consuming the food categories of short grass (all weights), tall grass (15g, 35g), and broadleaf plants/small insects (15g, 35g).

Table 17 Small Mammal RQ Summary: 0.375lb ai/A

Risk Quotients based on Kenaga upper bound EEC	*Acute dose-based RQs*			Chronic dose-based RQs			Chronic dietary-based RQs
	15 g	*35 g*	*1000 g*	*15 g*	35 g	1000 g	All mammals
Short grass	0.10[b]	0.08	0.05	3.12[c]	2.67[c]	1.43[c]	0.36
Tall grass	0.05	0.04	0.02	1.43[c]	1.22[c]	0.66	0.17
Broadleaf plants/ small insects	0.06	0.05	0.03	1.76[c]	1.50[c]	0.80	0.20
Fruits/pods/seeds/ lg insects	0.01	0.01	0.00	0.20	0.17	0.09	0.20
Seeds (granivores)	0.00	0.00	0.00	0.04	0.04	0.02	NA

[a] exceeds acute risk LOC (0.5)
[b] exceeds endangered species acute risk LOC (0.1)
[c] exceeds chronic risk LOC (1.0)

PLANTS

For both proposed uses of fomesafen, ground application at 0.5 lb ai/A and aerial application at 0.375 lb ai/A, total loading RQs exceeded the acute plant risk LOC (1) for both monocots and dicots in adjacent wetland areas but not in upland areas (Table 18). Drift-based RQs were exceeded for dicots in all adjacent areas. LOC exceedences for acute risk to endangered plants followed the same pattern, but were of greater magnitude. RQs based on the two alternative ground application scenarios (0.375 lb ai/A and 0.2 lb ai/A) were also generated. At both these rates, there were no exceedences for monocots. RQs for both total loading to wetland areas and drift only exceeded the acute risk and endangered species acute risk LOCs for dicots.

Table 18 Terrestrial Plant Risk Quotients Based on TerrPlant

Application Method	Total Loading RQ (Seedling emergence)		Total Loading RQ (Seedling Emergence)		Drift RQ (Vegetative vigor)	
	Upland areas		Wetland areas		All areas	
	Monocot	Dicot	Monocot	Dicot	Monocot	Dicot
Acute risk						
Use at 0.2 lb ai/A (alternative)						
Ground	0.07	0.08	0.47	0.53	0.01	2.04[a]

Use at 0.375 lb ai/A						
Aerial	0.29	0.33	1.05 [a]	1.19 [a]	0.06	11.72 [a]
Ground (alternative)	0.13	0.14	0.88	1.00 [a]	0.01	2.34 [a]
Use at 0.5 lb ai/A						
Ground	0.17	0.19	1.16 [a]	1.30 [a]	0.02	3.06 [a]
Endangered species acute risk						
Use at 0.2 lb ai/A (alternative)						
Ground	0.07	0.08	0.47	0.53	0.01	1.25 [a]
Use at 0.375 lb ai/A						
Aerial	0.29	0.33	1.05 [a]	1.19 [a]	0.08	19.13 [a]
Ground (alternative)	0.13	0.14	0.88	1.00 [a]	0.02	3.83 [a]
Use at 0.5 lb ai/A						
Ground	0.17	0.19	1.16 [a]	1.30 [a]	0.02	5.00 [a]

[a] Exceeds or equals LOC of 1

FUTURE DECISIONS

The Agency does not foresee requiring any additional ecological effects or environmental fate data listed in 40 CFR Part 158 prior to support current assessments. The Agency is re-reviewing environmental fate studies for fomesafen. These studies were re-reviewed because there was no documented assessment of degradation kinetics. The re-reviewed studies are not expected to alter the interpretation on the persistence of fomesafen in aquatic and soil environments. More importantly, the Agency needs to conduct an endangered species assessment due to the high phytoxicity of fomesafen.

IV. HUMAN HEALTH EFFECTS SCOPING DOCUMENT

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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

February 28, 2007

MEMORANDUM

SUBJECT: **Fomesafen Sodium**: HED Registration Review Problem Formulation Document.
PC Code:123802, DP Barcode: D306022.

FROM: Whang Phang, Toxicologist
Reregistration Branch 1
Health Effects Division (7509P)

THROUGH: Michael S. Metzger, Branch Chief
Reregistration Branch 1
Health Effects Division (7509C)

TO: Wilhelmena Livingston, Chemical Review Manager
Special Review and Reregistration Division (7508P)

Attached is the Health Effects Division chapter of the fomesafen sodium problem formulation document in supporting the registration review of this chemical.

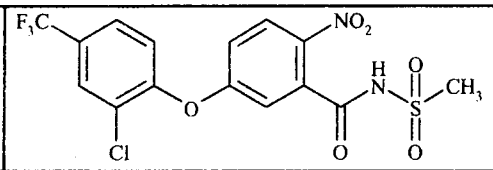
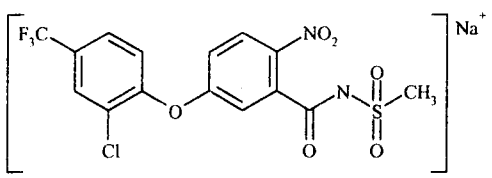
Section 1. Introduction

The HED Fomesafen Registration Review Team has evaluated the human health assessments for the herbicide fomesafen to determine the scope of work necessary to support the registration review. The team considered the current use profile, the toxicity, and exposure databases for this chemical. The primary source for the status update was the most recent HED human health risk assessment (Donna Davis, D325797, 2/28/06). The purpose of this screen is to determine whether sufficient data are available to assess the safety of this pesticide and whether any new data have been submitted since the last assessment which would necessitate conducting a new human health risk assessment to support registration review. A comprehensive listing of the documents considered is presented in Section 12 of this document. The HED Registration Review team includes Donna Davis, Toiya Goodlow, Matt Lloyd, and Whang Phang.

Fomesafen is currently registered for use on several crops including cotton, dry beans, snap beans, and soybeans. Tolerances are established in 40 CFR 180.433 for these commodities. Fomesafen is not registered for use on any sites that would result in residential exposure.

Section 2. Chemical Identity

Table 1. Fomesafen and its Sodium Salt Nomenclature

Chemical structure	
Common name	Fomesafen
Molecular formula	$C_{15}H_{10}ClF_3N_2O_6S$
Molecular weight	438.77
PC Code	N/A
IUPAC name	5-(2-chloro-α,α,α-trifluoro-p-tolyloxy)-N-methylsulfonyl-2-nitrobenzamide
CAS name	5-[2-chloro-4-(trifluoromethyl)phenoxy]-N-(methylsulfonyl)-2-nitrobenzamide
CAS registry number	72178-02-0
Chemical structure	
Common name	Sodium salt of fomesafen
Molecular formula	$C_{15}H_9ClF_3NaN_2O_6S$
Molecular weight	460.75
PC Code	123802
IUPAC name	5-(2-chloro-α,α,α-trifluoro-p-tolyloxy)-N-methylsulfonyl-2-nitrobenzamide, sodium salt
CAS name	5-[2-chloro-4-(trifluoromethyl)phenoxy]-N-(methylsulfonyl)-2-nitro-benzamide, sodium salt
CAS registry number	108731-70-0

Section 3. Toxicology

Fomesafen has low acute toxicity by oral route of exposure. It is severely irritating to the eye and is a moderate skin irritant. In the subchronic and chronic feeding studies, the consistent finding is the effect in the liver characterized by increases in liver weight and in associated enzymes including alkaline phosphatase, alanine transaminase, and aspartate transaminase. Hyalinization of the liver is also observed.

Currently, the toxicity database is adequate in establishing the toxicity endpoints for risk assessment. No toxicity studies have been received since the last human health risk assessment (D. Davis, D325797, 2/28/06). Acute inhalation and dermal toxicity studies and a skin sensitization study were identified as data gaps.

The risk assessment team has reevlauated the toxicity endpoints and doses according to the current policies on selecting toxicity endpoints and uncertainty factors. These conclusions are summarized below.

Cancer classification: The Cancer Assessment Review Committee (CARC) has classified fomesafen as "Not Likely to be Carcinogenic to Humans". A quantitative cancer risk assessment is not needed.

FQPA safety factor: Based on the available toxicology data, the fomesafen risk assessment team recommended the FQPA SF be reduced to 1x because there was no concern and/or residual uncertainty with regard to pre- and/or postnatal toxicity. Since no new data are available to necessitate any changes to this conclusion and it concurs with the current FQPA policy, the conclusion remains unchanged.

Table 2. Summary of Toxicological Doses and Endpoints for Fomesafen for Use in Human Risk Assessments

Exposure Scenario	Point of Departure	Uncertainty/ FQPA Safety Factor	RfD, PAD, Level of Concern for RA	Study and Toxicological Effects
Acute Dietary (females 13-49) and General population	No toxic effects attributable to a single dose of fomesafen were found in the database.			
Chronic Dietary (all populations)	NOAEL = 0.25 mg/kg/day	UF_A = 10x UH_H = 10x FQPA SF = 1x	RfD = 0.0025 mg/kg/day cPAD = 0.0025 mg/kg/day	Chronic toxicity - rat LOAEL = 5 mg/kg/day based on hyalinization of the liver in males
Dermal Short-Term (1-30 days)	NOAEL = 100 mg/kg/day	UF_A = 10x UH_H = 10x FQPA SF = 1x	LOC for MOE = 100 (Occupational)	Prenatal developmental – rat LOAEL = 200 mg/kg/day based on postimplantation loss

Table 2. Summary of Toxicological Doses and Endpoints for Fomesafen for Use in Human Risk Assessments				
Exposure Scenario	**Point of Departure**	**Uncertainty/ FQPA Safety Factor**	**RfD, PAD, Level of Concern for RA**	**Study and Toxicological Effects**
and Intermediate-Term (1-6 months)	(Dermal absorption rate = 20%)*			
Inhalation Short-Term (1 - 30 days) and Intermediate-Term (1-6 months)	NOAEL = 0.5 mg/kg/day (Inhalation adsorption rate = 100% oral equivalent)	UF_A = 10x UH_H = 10x FQPA SF = 1x	LOC for MOE = 100 (Occupational)	90-Day - rat LOAEL = 10 mg/kg/day based on hyalinization of hepatocytes, increased eosinophilia, reduced granulation, increased liver weights in males and females, and increases in plasma alkaline phosphatase, alanine transaminase and aspartate transaminase in males.
Cancer Classification	"Not Likely to be Carcinogenic to Humans."			

NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UH_H = potential variation in sensitivity among members of human population (intraspecies). FQPA SF= FQPA safety factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure. LOC = level of concern. RA = risk assessment

* = The dermal absorption factor was estimated to be 20% based on the results of structurally related chemicals: acifluorfen (20% absorption rate) and oxifluorofen (18% absorption rate).

Section 3. Residue Chemistry

The residue chemistry database is essentially complete except for supporting data required as a condition of registration for certain new uses (D. Davis, D325797, 2/28/2006). The supporting data are listed in the Attachment.

Section 4. Dietary Exposure

Acute dietary risk assessments were not required as there were no endpoints identified attributable to a single exposure of fomesafen. Chronic dietary risk assessments were conducted for fomesafen sodium using the Dietary Exposure Evaluation Model (DEEM-FCID™), Version 2.03, which used food consumption data from the United States Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The assumptions of these assessments were tolerance level residues and 100% crop treated. The highest exposure and risk estimates based on exposure from food only were for the "children 1 - 2 years" population subgroup. The exposure for food was 0.000041 mg/kg/day, which utilized 1.6% of the cPAD (chronic population adjusted dose).

Section 5. Aggregate and Cumulative Exposure

There are no residential uses formulated with fomesafen. Therefore, the aggregate assessment considers only chronic exposure for food and drinking water.

An aggregate dietary assessment using DEEM-FCID™ was conducted in which the estimated drinking water concentrations (EDWCs) for ground and surface water from the Environmental Fate and Effects Division were included directly in the assessment (Table 3). The dietary exposure analyses in this assessment resulted in chronic dietary risk estimates for food and water that were below the Agency's level of concern. The highest exposure and risk estimates were for the "all infants" population subgroup. The exposure for food plus surface water was 0.000766 mg/kg/day, which utilized 31% of the cPAD; and the exposure for food plus ground water was 0.000107 mg/kg/day, which utilized 4.3% of the cPAD.

Table 3. Summary of Chronic Dietary Exposure and Risk for Fomesafen Sodium Incorporating Food and Surface and Ground Water As Drinking Water Sources

Population Subgroup [1]	Surface Water			Ground Water		
	EDWC (ppb)	Exposure (mg/kg/day)	% cPAD	EDWC (ppb)	Exposure (mg/kg/day)	% cPAD
General U.S. Population	10.535	0.000239	9.5	1.0	0.000038	1.5
All Infants (< 1 year old)	10.535	**0.000766**	**31**	1.0	**0.000107**	**4.3**
Children 1-2 years old	10.535	0.000371	15	1.0	0.000072	2.9
Children 3-5 years old	10.535	0.000344	14	1.0	0.000064	2.6
Children 6-12 years old	10.535	0.000236	9.4	1.0	0.000044	1.7
Youth 13-19 years old	10.535	0.000175	7.0	1.0	0.000030	1.2
Adults 20-49 years old	10.535	0.000221	8.8	1.0	0.000033	1.3
Adults 50+ years old	10.535	0.000231	9.2	1.0	0.000033	1.3
Females 13-49 years old	10.535	0.000219	8.8	1.0	0.000032	1.3

[1] The values for the population with the highest dietary exposure and risk estimates are bolded.

Section 6. Occupational Exposure

There is potential for occupational exposure to fomesafen during mixing, loading, application, and postapplication activities. The occupational database is adequate, and all relevant occupational scenarios are assessed for all existing uses. The latest risk assessment (M. Lloyd, D294458, 2/15/2006) indicated most of the occupational scenarios did not result in risks of concern, with the exception of inhalation risks to mixer/loader scenario for aerial application. Inhalation MOEs for the mixer/loader scenarios for aerial application were of concern with baseline PPE (includes long-sleeve shirt, long pants, and gloves). PF5 respirators are required to achieve acceptable MOEs (i.e., greater than the target MOE of 100). All of the dermal MOEs are greater than the target MOE of 100 with single layer PPE for handlers and baseline PPE for applicators and flaggers. Single layer PPE is mandated on the proposed fomesafen label under

consideration. All of the post-application MOEs are greater than 100 on Day 0, and the risks are not of concern.

Section 7. Incident Report of human Health Effects Caused by Fomesafen.

The available incident report data bases (1982 to the present) indicate skin irritation in four cases and no reports of other ill effects (M. S. Hawkins, D331945, 7/25/2006).

Section 8. Anticipated Data Needs

HED anticipates that a revised risk assessment for fomesafen will not be needed for registration review. Additional data have been previously required as conditions of registration for certain new uses. These are listed in the Attachment to this document for informational purposes.

Section 10. Tolerances

Tolerances are established under 40 CFR §180.433 for the residues of fomesafen 5-[2-chloro-4-(trifluoromethyl) phenoxy]-N-(methylsulfonyl)-2-nitrobenzamide from the application of its sodium salt as shown in the table below.

No Codex maximum residue limits (MRLs) have been established for residues of fomesafen. Canadian MRLs have been established for residues of fomesafen in/on dry beans, lima beans, snap beans, and soybeans at 0.05 ppm.

Commodity	U.S. (ppm)	Codex (mg/kg)	Canada (ppm)
Soybean	0.050		0.05
Cotton, undelineated seed	0.025		
Cotton, gin byproducts	0.025		
Bean dry	0.025		0.05
Bean, snap, succulent	0.025		0.05
Lima beans			0.05

Section 11. Overall Conclusions

HED anticipates no additional human health risk assessments will be needed for the existing uses of fomesafen.

Section 12. Reference Memoranda

The memoranda listed in the following table were considered in the development of this document.

HED Memoranda Relevant to Registration Review			
Author	**Barcode**	**Date**	
D. Davis	D325797	2/28/06	Fomesafen Sodium. Human Health Risk Assessment for a Proposal to Amend Use on Soybeans, and Proposal to Add uses on Cotton, Dry Bean, and Snap Bean.
D. Davis		4/25/06	Fomesafen Sodium. Addendum to the 2/28/02 Human Health Risk Assessment for a Proposal to Amend Use on Soybeans, and Proposal to Add uses on Cotton, Dry Bean, and Snap Bean.
J. Kidwell	TXR # 0053835	11/3/05	Second report of the Cancer Assessment Review Committee
M. Lloyd	D294458	2/15/06	Fomesafen: Occupational and Residential Exposure and Risk assessment for the Registration for New Uses on Dry Beans, Snap Beans, and Cotton.
T. Goodlow	D325798	2/15/06	Chronic Dietary Exposure Assessment for the HED Human Health Risk Assessment.
W. Greear	TXR # 0052977	1/20/06	Fomesafen: Toxicological Assessment for Incorporation into Risk Assessment Document.
D. Davis	D325801	4/25/06	Fomesafen Sodium: Residue Chemistry Summary for Human Health Risk Assessment, a Proposal to Amend use on Soybeans, and Proposals to Add uses on Cotton, Dry Bean, and Snap Bean.
J. Hetrick	D314014	9/27/05	Tier II Drinking water Assessment for Fomesafen use on cotton, soybeans, dry beans, and snap beans.

Attachment

This list represents data previously required as a condition of registration for certain new uses. This is provided for information purposes only.

1. Upgrade the cotton metabolism study with additional information (actual application rate for higher treatment rate, date of sample analysis).

2 Submit raw data to support the submitted method validation data.

3 Modifications for enforcement method to incorporate specific information on dry bean, snap bean, and soybean aspirated fraction.

4. Submit multiresidue method testing data for fomesafen.

5. Data on the stability of residues of fomesafen in/on cotton gin byproducts, soybean hulls and oil, and field corn or sorghum forage & stover.

6. Additional data to upgrade the available cotton crop field trial data including soil characteristic data, summary of weather conditions at individual sites, indications as to whether irrigation was used, & average historical data for temperature & rainfall for the duration of the field trial intervals.

Guideline 869.1200 Acute dermal toxicity study
Guideline 870.1300 Acute inhalation toxicity study
Guideline 869.2600 Skin sensitization study

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)
TGAI	Technical Grade Active Ingredient
USDA	United States Department of Agriculture
UF	Uncertainty Factor
WPS	Worker Protection Standard