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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DP Barcode: D290065, D290068, D290076,
305000 and D311730
PC #: 123009

Date: May 12, 2005

Memorandum

SUBJECT: New Chemical Registration
Topramezone (BAS 670H) Ecological Risk Assessment
and End-use Product "BAS 670 336SC Post Emergent Corn Herbicide"
CAS Reg. No. 210631-68-8

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Enclosed please find the Ecological Risk Assessment for the new chemical topramezone and the proposed end-use product "BAS 670 336SC Post Emergent Corn Herbicide" (29.7% topramezone). Proposed uses are on field corn, seed corn, popcorn, and sweet corn. The Drinking Water Assessment was submitted to the Health and Effects Division in April 3, 2005 under the DP Barcode D314642.

Although belonging to different chemical families, topramezone shares the same mode of action as isoxaflutole and mesotrione. These three chemicals inhibit the biosynthesis of carotenoids by inhibiting the enzyme 4-hydroxyphenyl-pyruvate dioxygenase (4-HPPD). Therefore, topramezone is expected to cause similar effects in non-target plants as isoxaflutole and mesotrione. In addition, 4-HPPD inhibitors disrupt the catabolism of tyrosine.

The seasonal maximum recommended application rate of topramezone is 0.022 lb a.i. per acre (25 g/ha). Single or two split applications seven days apart may be used, but not to exceed the maximum seasonal application rate. Aerial and ground applications are being proposed. The ecological risk assessment of topramezone was based on the use information provided in the proposed label, dated December 2004.

1. Topramezone as a Joint Review with Canada

Topramezone underwent a joint review with Canada's PMRA under a NAFTA agreement. The primary review of Environmental Fate studies was the responsibility of the USEPA, but the primary review of the ecological effect studies was performed by PMRA. The Data Evaluation Records (DER) were exchanged for secondary review by the two agencies in order to agree on the validity, significance, and deficiencies of the studies.

For the Environmental Fate studies, several deficiencies were identified for the aerobic and anaerobic water-sediment studies and for the frozen storage stability study conducted to support the terrestrial field dissipation data. The Agency and PMRA prepared a joint request to the petitioner to obtain additional information or clarification that could be used to upgrade the studies and improve the ecological risk assessment of topramezone. The data requests are attached to this Transmittal Memorandum. All of the requested data and information are of high importance for improving the present risk assessment.

Deficiencies of the ecological effect studies were identified for avian subacute dietary, avian reproduction, daphnid life cycle, seedling emergence and vegetative vigor. The requested information are of moderate to low importance for improving the topramezone risk assessment.

2. Ecological Risk Conclusions

<u>Plants</u>

a. *Terrestrial*

The EFED assesses risk to terrestrial plants at two different stages of development. Risk to emerged plants is assessed from drift exposure compared to the results of the vegetative vigor studies. Risk to seeds germinating and emerging through soil is assessed from exposure from runoff plus drift compared to the results of the seedling emergent study.

(3)

Vegetative vigor is a more sensitive endpoint than seedling emergence for topramezone. Therefore, even though exposure from drift alone is lower, in lb ai/acre, than drift plus runoff, the RQ for exposure from drift is higher, because the lowest EC_{25} (0.0001 lb ai/acre) and EC_{05} (0.000009 lb ai/acre) from vegetative vigor tests was much lower than the seedling emergence EC_{25} (0.0039 lb ai/acre) and NOAEC (0.0017 lb ai/acre) for seedling emergence.

Table 1. Summary of LOC exceedances for non-endangered terrestrial plants.			
Habitat and exposure route	Plant stage	Aerial	Ground
Terrestrial plants in dryland areas receiving drift and runoff	seed germination and seedling emergence	LOC not exceeded RQ<1	LOC not exceeded RQ<1
Terrestrial plants in semi-aquatic areas receiving drift and runoff	seed germination and seedling emergence	**LOC exceeded RQ=1.9**	**LOC exceeded RQ=2.8**
Areas adjacent to treated area receiving drift	vegetative vigor of emerged plants	**LOC exceeded RQ=11**	LOC not exceeded RQ<1

Table 2. Summary of LOC exceedances for endangered terrestrial plants.			
Habitat and exposure Route	Plant growth stage	Aerial	Ground
Terrestrial plants in dryland areas receiving drift and runoff	seed germination and seedling emergence	**LOC exceeded RQ=1**	LOC not exceeded RQ<1
Terrestrial plants in semi-aquatic areas receiving drift and runoff	seed germination and seedling emergence	**LOC exceeded RQ=4.5**	**LOC exceeded RQ=6.6**
Areas adjacent to treated area receiving drift	vegetative vigor of emerged plants	**LOC exceeded RQ=122**	**LOC exceeded RQ=24**

A further evaluation of the Risk Quotients suggest that terrestrial dicots may be potentially at a higher risk than monocots. **Even though the LOCs were not exceeded for the terrestrial monocots, topramezone is recommended for the control of grasses. Therefore, risk to monocots to other non-tested species in terrestrial, dryland, and semi-aquatic habitats cannot be ruled out.**

The vegetative vigor studies were not conducted with an adjuvant, as per label recommendation. Therefore, the effects on non-target plants may be more pronounced when an adjuvant is incorporated into the spray solution. This has been identified as a data gap.

b. *Aquatic*

The primary route of exposure for aquatic plants is runoff. Drift was shown not to be a significant exposure route. Levels of Concern were exceeded for vascular endangered plants, with RQ ranging from 1.15 to 1.94, depending on the location of the corn scenario used in estimating environmental concentrations in surface water. Levels of Concern were not exceeded (RQ < 1) for non-endangered non-vascular plants and for endangered non-vascular plants.

Animals

No Levels of Concern were exceeded for acute and chronic risks associated with avian, mammal, fish, and invertebrate exposures to topramezone. Thus, minimal risk on an acute exposure basis is expected for birds, mammals, fish and invertebrates including reptiles and amphibians. However, some effects were observed in laboratory studies that suggest potential chronic effects.

Endocrine Disruptor Potential

The EFED is recommending this chemical for future screening in the Endocrine Disruptor Screening Program (EDSP) in order to better characterize any topramezone effects related to endocrine disruption in wildlife and aquatic animals.

Topramezone showed some effects in laboratory studies, such as reduction in number hatched to viable embryos, hatchling body weight and female weight gain in birds, thyroid effects for mammal (thyroid tumors), reductions in weight and length of fish, and reductions of live offspring produced per female daphnid. In addition, topramezone showed eye effects, pancreatic effects, and skeletal variations typically caused by inhibition of the 4-HPPD enzyme.

c. Exposure Conclusions

Drift and/or runoff were identified as the routes leading to residues of topramezone in aquatic ecosystems. Drift and/or runoff , as well as post-treatment residues in soils, can be associated as potential exposure routes for non-target terrestrial plants. Inadvertent residues of topramezone can also be present in irrigation water and may be phytotoxic to irrigated non-target plants. In addition, soils containing residues of topramezone have the potential to be transported off-site by airborne dust or soil erosion. Recommended rotational crop intervals greater than 18 months suggest that residues of topramezone in soil are still active and may cause injury to sensitive, non-target plants.

Environmental Fate

Topramezone can be persistent in aerobic soils (half-life >125 days). Although formation of metabolites involve microorganisms, dissipation of topramezone in the environment appears to be predominantly controlled by time-dependent sorption. Even though the batch-equilibrium adsorption/ desorption studies indicate that topramezone may be very mobile in some soils/sediments, increasing non-extractable residues with time provides evidence for time-dependent sorption behavior. Intact residues of topramezone may remain associated with the humic material and/or mineral components in soils and pose a potential to accumulate from season to season. Slow desorption may free topramezone residues and extend the phytotoxicity of the soils. Neither abiotic hydrolysis nor direct photolysis in water nor photolysis on soil are significant dissipation routes for topramezone.

Metabolites of Concern

Two metabolites of topramezone (M670H01 and M67010)[1] share the same molecular structure features that are associated with inhibition of 4-HPPD. Therefore, these two metabolites have the potential to exhibit herbicidal activity. Moreover, M670H01 (the cyano metabolite) has molecular structure features that resemble a very persistent degradate of isoxaflutole (RPA-202248) believe to be the herbicide-active chemical species of isoxaflutole. Both M670M01 and RPA-202248 are "diketonitriles". There are no ecological toxicity data for these two metabolites of topramezone.

Environmental Concentrations in Aquatic Ecosystems

The aquatic exposure assessment was performed only for parent topramezone. Ten corn scenarios were used to estimate environmental concentrations of topramezone in surface water using Tier II PRZM and EXAMS simulation models. All of the peak concentrations were below 2 μgL^{-1} (2 ppb).

The sensitivity of an available analytical chemistry method to identify and quantify residues of topramezone in water is not adequate. The Limit of Quantitation (LOQ) of this method is 60 μgL^{-1} (ppb) whereas Levels of Concern for aquatic vascular plants were triggered at concentrations of $< 2\ \mu gL^{-1}$, which is well bellow this LOQ. Thus, this method cannot quantify residues of topramezone at concentrations triggering Levels of Concern for aquatic vascular plants. This analytical chemistry method cannot be used for monitoring or enforcement.

The highest environmental concentrations were for the Florida sweet corn scenario. Florida is a leading state in sweet corn production, were sweet corn is predominantly grown around the Everglades and where many carotenoid rich plants can grow in nearby fields (e.g., citrus fruits; tomatoes). Florida sweet corn is potentially a vulnerable use site for topramezone

[1]"M670H01" was a major metabolite in some aerobically incubated soils and in one aerobic water-sediment system."M670H10" is only formed under anaerobic conditions.

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d. Ecological Effects Conclusions

As expected for a herbicide, the major effects were on plants. For aquatic plants, toxic effects were higher on vascular than on non-vascular plants. Vascular plants are more sensitive to topramezone (TGAI) than to M670H05 (metabolite) or to BAS 670 00H (formulated topramezone). The most pronounced effects on frond counts were observed for topramezone TGAI. No tests were conducted with "M670H01" or "M670H10", which may exhibit herbicidal activity.

All terrestrial plants showed toxic effects in seedling emergence and vegetative vigor studies, but at varying degree depending on the species and exposure concentrations. In seedling emergence and vegetative vigor studies, monocots were observed to be less sensitive than dicots. The most sensitive plants to seedling emergence were ryegrass (monocot) and cabbage (dicot). The most sensitive plants to vegetative vigor were onion (monocots) and soybeans (dicots). Dry weight was selected as the most sensitive endpoint. However, phytotoxic effects and other growth effects such as shoot height were also observes.

Overall, topramezone is practically nontoxic to avian, mammalians, honeybees, earthworms, freshwater fish and invertebrates and estuarine/marine fish and moderately toxic to estuarine/marine invertebrates. Chronic effects for bobwhite quail reproduction include reduction in the ratio of number hatched to live embryos (a measure of hatchability) at the highest treatment level, 1012 mg ai/kg dw and the mallard duck reproduction had significant reductions in hatchling body weight and female weight gain at all three treatment levels, resulting in the inability to define a NOAEC. No chronic effects were observed in mammals as high as 4000 ppm, based on a two-generation toxicity study on laboratory rats. Chronic effects were apparent for freshwater fish with reduced growth (length and weight) at 9.01 mg aiL-1. Estimated chronic effects for estuarine/marine fish are uncertain because no chronic data were submitted by the registrant; therefore, the NOAEC value was derived based on the assumption that the freshwater and estuarine/marine fish are of equal sensitivity.

M670H05 is practically nontoxic to freshwater fish and invertebrates. The formulated product BAS 670 00H is practically nontoxic to honeybee, terrestrial invertebrates, and freshwater fish and invertebrates.

e. Uncertainties

a. Aquatic exposure- The aerobic aquatic metabolism half-life is an important input parameter used in simulation models (PRZM-EXAMS; FIRST; GENEEC) to estimate environmental concentrations in surface water. The submitted studies have multiple deficiencies and questionable results that prompted the use of the recommended default value for PRZM and EXAMS estimates (2 x the aerobic soil metabolism half-life of 241 days). Therefore, the uncertainty on the persistence of topramezone in aerobic water-sediment systems is carried over the model-estimated concentrations.

b. The toxicity of the metabolites M670H01 and M670H10 is not known. Both metabolites share molecular structure features with topramezone and other 4-HPPD inhibitors.

c. Terrestrial plant toxicity tests were not conducted with any of the metabolites of topramezone. Therefore, the effect of metabolites on terrestrial plants is unknown.

d. The proposed label requires that the product add an adjuvant and a nitrogen fertilizer to achieve optimum weed control. Vegetative vigor studies designed to address the adjuvant or fertilizer of the post-emergence herbicide on non-target plants are uncommon. Data on BAS 670 00H with both the adjuvant and fertilizer on non-target plants should be submitted to better understand the potential effects to non-target plants.

e. Thyroid effects were identified for the test mammals. Topramezone is an inhibitor of the 4-HPPD enzyme. In mammals, this inhibitory behavior affects the catabolism of tyrosine. How this effects manifests in wild mammals is not known.

6. Recommended Changes in the Proposed Label for the End-use Product

According to the label, the soil should not be disturbed between the split applications. The petitioner is requested to explain the reason for this.

Identification of Data Gaps

Environmental Fate

Topramezone is a NAFTA Joint Review with Canada. Both PMRA and the USEPA identified

Identification of Data Gaps

Environmental Fate

Topramezone is a NAFTA Joint Review with Canada. Both PMRA and the USEPA identified deficiencies in the studies that must be addressed by the petitioner. The importance of needed data is discussed in this section. In addition, the registrant should formally petition waivers for the 163-2, Volatilization from Soil and 165-4, Bioaccumulation in Fish, Subdivision N Data Requirements. Neither the vapor pressure nor the Log *n*-octanol-water partition coefficient trigger the requirements for this studies.

Aerobic Soil Metabolism (162-4)

David, M.D.2002. *BASF 670 H: Aerobic Aquatic Metabolism*. Performed by BASF Corp., Ewing, NJ. BASF Report ENV 01-055. BASF Study 56940. BASF Re. Document # 2002/5003947. Completed on 6/28/2002
45902423

Deficiency	Required	Importance
Topramezone was much less persistent in the pond water-sediment (19 to 24 days in the whole system) than in the river-water sediment (> 120 days). The chemical and physical characteristics of the two sediments were markedly different. The pond water-sediment appears to be atypical: the sediment had a very low pH, the water had a high electrical conductivity and high amount of "dissolved" solids. These characteristics are reminiscent of ponds receiving acid mine drainage	It is requested that an attempt be made to satisfactorily address these differences. Otherwise, a new study may be required	The importance of this request is **HIGH.** Aerobic soil metabolism half-life is an important input parameter to estimate exposure concentrations in aquatic ecosystems and in drinking water drawn from surface water. In the selection of input parameters for PRZM-EXAMS, assumptions had to be made for the most conservative case by using twice the already prolonged aerobic soil metabolism half-life of241 days. The exposure concentrations in aquatic ecosystems may represent an overestimate. This, in turn, may overestimate the risk to aquatic plants and to irrigated crops. In addition, the metabolite "M670H01" identified in the pond water-sediment system has molecular structure feature that suggest that it potentially manifest the same mode of action as topramezone. The amount of this metabolite in this system may not reflect its concentration in less atypical systems.

(8)

Anaerobic Aquatic Metabolism (162-3)

Guirguis, A. 2002*Anaerobic Aquatic Metabolism of ^{14}C-BAS 670 H.*Conducted by BASF, Research Triangle Park, NC.and BASF Aktiengesellshaft, Limburgenhof, Germany.BASF Study No.58523. BASF Reg. Doc. 2002/5003696. Completed on 12/16/2002
USEPA 45902422

At this time, this study is not acceptable. However, it may be upgrade if the following deficiencies are adequately addressed by the petitioner.

Deficiency	Required	Importance
Individual replicate results for parent (BAS 670H) and its degradates (HPLC analyses) were only provided for five of the ten sampling intervals, and there were sufficient levels of variability between replicates at the same sampling interval and between means for consecutive sampling intervals. The validity of the reported results could not be confidently assessed due to these sufficient variability between replicates	1. Submit additional replicate data. 2. Provide a rationale explaining these variability	**HIGH** A degradate (M670H10) identified in this study has been identified as potentially exhibiting the same herbicidal mode of action as topramezone. The additional data may clarify the concentrations of this metabolite at each sampling time.
Storage conditions and intervals of sediment samples prior to and after extraction and of sediment extracts and water layers prior to analysis were not reported and it was not established that the variable results were not the consequence of instability during storage prior to analysis.	1. Submit information on storage procedures and intervals of sediment sampling 2. Provide a rationale explaining these variability	Same as above
It was not established that the methodology employed did not artificially degrade parent BAS 670H and it transformation products.	Method validation data is required to ensure that the extraction and concentration techniques employed did not effect on the integrity (transformation) of BAS 670H prior to analysis	Same as above
All degradates detected at ≥10% of the applied radioactivity have not been identified. An unidentified compound, Unk1 (Rt 6:27), was detected in phenyl-U-^{14}C -lable treated sediment at a mean of 8.55% of the applied. Because the concentration of this compound is very close to ≥10% of the applied the applicant must submit the replicate results. This compound must be identified.	1. Submit the replicate results 2. Unk1 compound must be identified	**HIGH** Unknown 1 may have molecular structure features that could suggest potential herbicidal activity

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Mobility in Soils (163-1)

In all of the studies involving soils and sediments, the increase in "non-extractable" radioactive residues increased with time and were mostly associated with the fulvic acid fraction. Thus, the overall dissipation of topramezone appears to be controlled by the kinetics of sorption rather than by biotransformation (i.e., time-dependent adsorption and desorption). That is, a competition between sorption and transformation. Unfortunately, studies designed to address the kinetics of adsorption and desorption of pesticides on soils/sediment are not commonly conducted. Data on kinetics of adsorption/desorption of topramezone should be submitted, if available. These data may help assessing the contribution of time-dependent sorption over biotransformation.

Frozen Storage Stability

White , M. And K. Smith. 2003. *Freezer storage stability of BAS 670H and its degradates in soil.* Document No. 2002/5004331. BASF study No. 59941. Completed on 12/31/2003. **45902428**

The quality of a terrestrial field dissipation study depends on the stability of residues in the samples taken from the field and analysis. The following deficiencies were identified in this study.

Deficiency	Required	Importance
The method by which the soil was treated was not described, so the potential for treatment variability could not be assessed.	Provide information on the soil treatment method.	**HIGH** for further evaluating the terrestrial field dissipation studies
The mean incubation temperatures was reported, however, no data supporting these values was provided	Submit supporting data for temperature (min. and max.temperatures).	Same as above
The detailed description of the HPLC/MS method was not provided.	Submit detailed description of the HPLC/MS method	Same as above
The soil samples for different intervals were not treated on the same date. The 0-day samples were treated on 2/4/02, the 4-month samples on 10/9/01, and the longer stored samples (range of 18 to 29.5- month) on 8/4/00. Therefore, the samples identified as "time zero" can not serve as a baseline for the stored samples and they can not be used to validate the application rate. Please note that this is not the preferred method for determining storage stability. A set of samples is treated, a subset is analyzed as time 0, and the remainder are stored frozen and sampled at various intervals. *All data appear to be reported in terms of percent of the nominal application rate*	1. Provide rationale as why the soil samples for different intervals were not treated on the same date and the treatment times are reverse than a typical storage stability study. 2. Provide measured data if available 3. Provide rationale for using nominal data instead of measured data	Same as above

Deficiency	Required	Importance
HPLC chromatograms were provided only for one 18-month sample	Provide chromatograms for later sampling intervals to demonstrate that no transformation products of BAS 670H were recovered from the soil	Same as above

Ecological Effects

Avian Subacute Dietary 71-2(a)

Zok, S. 2001. BAS 670 H - Avian dietary LC50 test in chicks of the Bobwhite quail (*Colinus virginianus*). Environmental Toxicology and Ecology, BASF Akiengesellschaft, 67056 Ludwigshafen/Rhein, Germany. Project No. 31W0124/98135. BASF Corporation. July 12, 2001. **45902310**

Deficiency	Required	Importance
Data verifying the stability of topramezone in treated feed were not provided. Topramezone was reported to be stable over 30 days in the diet, however, the analytical report (08B0124/986033) was not submitted for verification.	Provide the analytical report for verification	**LOW** for verifying the stability of test concentrations in treated feed.

Avian Reproduction 71-4(a)

Zok, D. 2002. BAS 670 H - 1-Generation reproduction study on the bobwhite quail (*Colinus virginianus*) by administration in the diet. Experimental Toxicology and Ecology, BASF AG, Germany. Unpublished. Project No. 71W0124/98086. BASF Registration No. 2002/1005238. **45902312**

Deficiency	Required	Importance
Stability of BAS 670 H at room temperature was verified for 30 days in treated quail feed prepared at 60 ppm only; this level is below the range of concentrations tested in the definitive study.	Provide data verifying the stability of BAS 670 H under actual use conditions.	**LOW** for verifying the stability of actual test concentrations in treated feed.

3. Avian Reproduction 71-4(b)

S. Zok. 2002. BAS 670 H - 1-Generation reproduction study on the mallard duck (*Anas platyrhynchus*) by administration in the diet. Environmental Toxicology and Ecology, BASF

Akiengesellschaft, 67056 Ludwigshafen/Rhein, Germany. Project No. 72W0124/98126. BASF Corporation. February 18, 2002
45902313

Deficiency	Required	Importance
1. Stability of BAS 670 H at room temperature was verified for 30 days in treated quail feed prepared at 60 ppm only; this level is below the range of concentrations tested in the definitive study. 2. All three concentrations tested elicited adverse effects on hatchling body weight and adult female weight gain; therefore, a NOEC could not be determined.	1. Provide data verifying the stability of BAS 670 H under actual use conditions. 2. A new study with concentrations lower than the tested concentrations to establish a NOAEC.	**MODERATE** for establishing a NOAEC and verifying the stability of actual test concentrations in treated feed.

4. <u>Aquatic Invertebrate Life-Cycle 72-4(b)</u>

Jatzek, H.-J. 2002. BAS 670 H - Determination of the chronic effect on the reproduction of the water flea *Daphnia magna* STRAUS. BASF AG, Germany. Study No. 01/0082/51/3. BASF Registration No. 2002/1008626.
45902320

Deficiency	Required	Importance
Dry weight of surviving daphnids was not measured.	Provide data on dry weight if available	**MODERATE** to determine the growth deficiencies of daphnids, if any

5. <u>Aquatic Plant Growth (Tier 2) 123-2</u>

Palmer, S.J., T.Z. Kendall, H.O. Krueger, and C.M. Holmes. 2001. BAS 670 H: A 96-hour toxicity test with the freshwater diatom (*Navicula pelliculosa*). Wildlife International, Ltd., Maryland, USA. Unpublished. Laboratory Study No. 147A-186. BASF Registration No. 2001/5002327.
45902332

Deficiency	Required	Importance
It was not possible to differentiate whether the reduction in diatom growth was due to topramezone, or from a reduction in pH.	Provide data with pH levels at 7.5 ± 0.1 at all treatment levels throughout the test, if available.	**LOW** to determine the toxicity of topramezone to freshwater diatoms

6. Seedling Emergence (Tier 2) 123-1(a)

In the seedling emergence study tested with BAS 670 00H, an end use product, exhibits toxicity effects to terrestrial plants. Thus, the toxic effects to terrestrial plants is known with the end use product only. In consideration of crop rotations, there are no terrestrial plant data to evaluate the phytotoxicity any of the metabolites of topramezone. The effect of metabolites on plants is not known. Data on toxicity of metabolites to seedling emergence (Tier II toxicity test) should be submitted, if available. The importance of the request is **moderate** to protect crop damage through crop rotation.

7. Vegetative Vigor (Tier 2) 123-1(b)

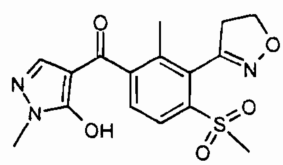
In the vegetative vigor study tested with BAS 670 00H, an end use product, exhibits toxicity effects to terrestrial plants. The proposed label requires that the product add an adjuvant and a nitrogen fertilizer to achieve optimum weed control. Thus, phytotoxic effects to terrestrial plants is known with the end use product without the adjuvant and fertilizer. Unfortunately, vigor studies designed to address the adjuvant or fertilizer of the herbicide on non-target plants are uncommon. Data on BAS 670 00H with both the adjuvant and fertilizer on non-target plants should be submitted, if available. The importance of the request is **moderate** to protect endangered plants from BAS 670 336SC.

ECOLOGICAL RISK ASSESSMENT

NEW CHEMICAL REGISTRATION

Topramezone (BAS 670H)

[3-(4,5-Dihydro-3-isoxazolyl)-2-methyl-4-(methylsulfonyl)phenyl]
(5-hydroxy-1-methyl-1H-pyrazol-4-yl) methanone
Chemical Family: Phenyl pyrazolyl ketone herbicide
CAS Registration Number: 210631-68-8
USEPA Chemical Code: 123009



Proposed End-Use Product: "BAS 670 336SC Post-emergent Corn Herbicide"
(29.7% topramezone)
Proposed Uses: Corn (grain, seed, popcorn, and sweet corn)

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I. Executive Summary

A. Nature of Chemical Stressor

Topramezone (BAS 670H; [3-(4,5-Dihydro-3-isoxazolyl)-2-methyl-4-(methylsulfonyl)phenyl](5-hydroxy-1-methyl-1H-pyrazol-4-yl) methanone) is a new post-emergence herbicide proposed for uses on corn (field corn, popcorn, seed corn, and sweet corn). Topramezone belongs to the phenyl pyrazolyl ketone family of herbicides. Its mode of herbicide action is inhibition of an enzyme (4-HPPD) that controls carotenoid biosynthesis. This is the same mode of action of isoxaflutole and mesotrione, although these two herbicides belong to different chemical families.

The proposed end-use product is "BAS 670 336SC Post-emergent Corn Herbicide" (29.7% topramezone). Aerial and ground applications are being proposed at a maximum application rate per season of 0.022 lb active ingredient per acre (25 g/ha) or two split applications seven days apart, but not to exceed 0.022 lb active ingredient per acre per season.

B. Potential Risks of Topramezone to Non-target Organisms: Animals and Plants

Topramezone is to be applied at a maximum application rate of 0.022 lbs ai/acre (25 g/ha) and is being proposed for ground and aerial applications. It was anticipated that non-target plants would be at risk. Minimal risk is expected for birds, mammals, fish and invertebrates including reptiles and amphibians

Direct Effects to Plants:

Vegetative vigor is a more sensitive endpoint than seedling emergence for topramezone. Therefore, even though exposure from drift alone is lower, in lb ai/acre, than drift plus runoff, the RQ for exposure from drift is higher, because the lowest EC_{25} (0.0001 lb ai/acre) and EC_{05} (0.000009 lb ai/acre) from vegetative vigor tests (soybeans) were much lower than the lowest seedling emergence EC_{25} (0.0039 lb ai/acre) and NOAEC (0.0017 lb ai/acre) (cabbage).

The vegetative vigor studies were not conducted with an adjuvant, as per label recommendation. Therefore, the effects on non-target plants may be more pronounced when an adjuvant is incorporated into the spray solution. This has been identified as a data gap.

A further evaluation of the Risk Quotients suggest that terrestrial dicots may be potentially at a higher risk than monocots. **Even though the LOCs were not exceeded for the terrestrial monocots, topramezone is recommended for the control of grasses. Therefore, risk to monocots to other non-tested species in terrestrial, dryland, and semi-aquatic habitats cannot be ruled out.**

Tables I.1 and I.2 summarize the Levels of Concern for non-endangered and **endangered** terrestrial plants.

Table I.1. Summary of LOC exceedances for non-endangered terrestrial plants (dicots)			
Habitat and exposure route	Plant stage	Aerial	Ground
Terrestrial plants in dryland areas receiving drift and runoff	seed germination and seedling emergence	LOC not exceeded RQ<1	LOC not exceeded RQ<1
Terrestrial plants in semi-aquatic areas receiving drift and runoff	seed germination and seedling emergence	**LOC exceeded RQ=1.9**	**LOC exceeded RQ=2.8**
Areas adjacent to treated area receiving drift	vegetative vigor of emerged plants	**LOC exceeded RQ=11**	LOC not exceeded RQ<1

Table 2. Summary of LOC exceedances for endangered terrestrial plants (dicots)			
Habitat and exposure Route	Plant growth stage	Aerial	Ground
Terrestrial plants in dryland areas receiving drift and runoff	seed germination and seedling emergence	**LOC exceeded RQ=1**	LOC not exceeded RQ<1
Terrestrial plants in semi-aquatic areas receiving drift and runoff	seed germination and seedling emergence	**LOC exceeded RQ=4.5**	**LOC exceeded RQ=6.6**
Areas adjacent to treated area receiving drift	vegetative vigor of emerged plants	**LOC exceeded RQ=122**	**LOC exceeded RQ=24**

Aquatic

The primary route of exposure for aquatic plants is runoff. Drift was shown not to be a significant exposure route. Levels of Concern were exceeded for vascular endangered plants, with RQ ranging from 1.15 to 1.94, depending on the location of the corn scenario used in estimating environmental concentrations in surface water. Levels of Concern were not exceeded (RQ < 1) for non-endangered non-vascular plants and for endangered non-vascular plants

C. Conclusions to the Exposure Characterization

Environmental Fate

Biotransformation (soils; water-sediments) is the major route of dissipation of topramezone in the environment, although it is slow with halflives from125 days to >1 year. However, there appears to be competition between biotransformation and sorption to soils/sediments in the overall dissipation of topramezone in terrestrial and water-sediment systems. Under environmental conditions, abiotic hydrolysis and direct photolysis in water are not important transformation pathways for topramezone. Topramezone exhibits high to moderate mobility in soils. Its major soil metabolite "M670H05" is highly mobile in soils. Topramezone is not expected to volatilize from soils or water nor to bioaccumulate in fish or other aquatic organisms.

Differences in persistence of topramezone, nature, and relative ratio of transformation products were found in six aerobic soils, but pseudo-first order, linear regression half-lives for topramezone were longer than 125 days. The major soil(> 10% of the applied radioactivity) metabolite is "M670H05" (3-(4,5-Dihydro-isoxazol-3-yl)-4-methanesulfonyl-2-methyl-benzoic acid), which could be persistent and accumulate in soils. In addition, if adsorption of topramezone on soils is considered as a dissipation route, topramezone residues on soils may have carryover potential from a growing season to the next. The metabolite 'MH670H01" ("cyano" metabolite) was found at > 10% only in one of six aerobic soils. Metabolites formed in aerobic soil were markedly different from those found in water-sediments (except "M670H01"). Metabolites were also distinctly different between anaerobic and aerobic water-sediments, but. deficiencies were identified in the water-sediment studies that must be addressed by the registrant to better understand the behavior of topramezone in water-sediment systems

Given the widespread cultivation of corn in the United States, there can be anticipated to be an extensive spatial and temporal variability in persistence, nature, and amount of biotransformation products of topramezone in soils.

Aquatic Ecosystems

Parent topramezone may enter a static water body by runoff and/or spray drift. Once in the water body, it may undergo biotransformation and/or adsorb to sediments, but how fast it adsorbs is not known, but is appears adsorption may control the dissipation of topramezone as opposed to biotransformation. The soil metabolite "M670H05" may reach surface water by runoff (or soil erosion), as this metabolite was not identified in water-sediment studies. The persistence of "M670H05" in water-sediment systems is not known. Exposure concentrations in surface water were estimated with the Tier II simulation models PRZM and EXAMS for ten different corn scenarios selected as surrogates to represent areas of potential use. Peak concentrations varied from 1.9 μgL^{-1} (Florida sweet corn) to 0.8 μgL^{-1} (East North Carolina). A major uncertainty affecting the confidence of the aquatic exposure concentration is the persistence of topramezone in water-sediment systems and how the physical and chemical characteristics of a water-sediment system may control the rate of dissipation.

The aquatic exposure assessment was performed only for parent topramezone. Ecological toxicity data with "M670H05" did not trigger a concern for aquatic organisms. No ecological toxicity data are available for "M670H01" and "M670H10". These metabolites were identified in water-sediment systems ("M670H01", aerobic; "M670H10", anaerobic) and have molecular structure features than suggest that they could exhibit the same mode of action as topramezone.

Terrestrial Ecosystems

Exposure in terrestrial ecosystems will occur through direct application to bird and mammal foraging food items in and immediately adjacent to the treated field. Based on the application rate, those residue levels will be relatively low compared to the acute and chronic toxicity to birds and mammals. Exposure to terrestrial and semi-aquatic ecosystems occupied by terrestrial plants will occur through drift and runoff. Exposure levels are likely to exceed levels of concern for terrestrial plants resulting in direct adverse effects to plants, and indirect effects are possible to animals depending on those plants for food, shelter and nesting structure.

D. Conclusions to the Effects Characterization

Topramezone is practically non-toxic to birds, mammals, fish, honeybees, earthworms, fish, but may be moderately toxic to marine/estuarine crustaceans. It is not expected to affect birds, mammals, fish or invertebrates chronically at levels that are expected in the field based on the relatively low application rate. Topramezone is toxic to aquatic and terrestrial plants. Nontarget terrestrial and aquatic plants would be at risk from off-site movement through drift and runoff.

There is some uncertainty in the chronic toxicity to birds. While the bobwhite study yielded a NOAEC of 294 ppm, the mallard study did not. There were small, but statistically significant reductions in body weight gain of offspring, and weight loss of adults, at the lowest level tested (100 ppm).

The EFED is recommending this chemical for future screening in the Endocrine Disruptor Screening Program (EDSP) in order to better characterize any topramezone effects related to endocrine disruption in wildlife and aquatic animals. Topramezone showed some effects in laboratory studies, such as reduction in number hatched to viable embryos, hatchling body weight and female weight gain in birds, thyroid effects for mammals, reductions in weight and length of fish, and reductions of live offspring produced per female daphnid. In addition, causes eye effects, pancreatic effects, and skeletal variations typically caused by inhibition of the enzyme 4-HPPD. Topramezone in an inhibitor of the 4-HPPD enzyme.

E. Uncertainties and Data Gaps

1. Exposure

Aquatic Exposure

The following factors can introduce uncertainties in the aquatic assessment. Some are identified as data gaps:

a. Topramezone is a weak acid (pKa 4.06). Above pH 5, the concentration of the anionic form increases and, theoretically, mobility will also increase. For example, the persistence and mobility of most sulfonylurea herbicides (also weak acids) have been found to increase with pH. However, the range of soil pH used in the aerobic soil metabolism and sorption studies conducted with topramezone as the test substance was quite narrow (5.7 to 6.9) and does not allow an adequate correlation of pH with mobility.

b. Persistence in water-sediment systems is not well established because of inherent flaws in the studies and/or inadequate selection of water-sediment systems. The petitioner has been asked to address specific issues identified in their data.

c. The estimated environmental concentrations (EECs) for aquatic exposure assessment was performed only for parent topramezone, but a qualitative assessment of other chemical species that might be in surface water was also included in the overall assessment. The only metabolite for which there are ecological toxicity data is "M670H05". However, two other metabolites (M670H01 and M670H10) have molecular features that suggest a mode of action similar to topramezone and other known 4-HPPD inhibitors.

d. It appears that there is competition between biotransformation and binding to soils/sediments, but which process controls the dissipation of topramezone cannot be satisfactorily established from the provided guideline studies. The guideline studies are not designed to estimate time-dependent adsorption/desorption (i.e., the kinetics of sorption). The significance is that these bound residues may be released later and prolong undesireable exposure.

e. The sensitivity of available analytical chemistry method to identify and quantify residues of topramezone in water is not adequate. The Limit of Quantitation (LOQ) of this method is 60 μgL^{-1} (ppb) whereas Levels of Concern for aquatic vascular plants were triggered at concentrations of < 2 μgL^{-1}, which is well bellow this LOQ. Thus, this method cannot quantify residues of topramezone at concentrations triggering Levels of Concern for aquatic vascular plants. This analytical chemistry method cannot be used for monitoring or investigations at ecologically significant exposure levels.

Terrestrial Exposure

An uncertainty in the exposure assessment is that for Tier 1 risk assessments, oral ingestion is the only route of exposure considered. Exposure by dermal and inhalation is not assessed. However to balance that, some fairly conservative assumptions are made in the exposure assessment that is conducted. For example, high end exposure levels are assumed, maximum application rates are used, for the tier one assessment, it is assumed that birds and mammals feed 100% on the food item (short grass) containing the highest expected residues. This tends to maximize the exposure level against which toxicity is compared. Therefore, the assessment is considered to be certain enough to identify direct toxicity, if it was likely. Other uncertainties as follows:

a. There is a potential for long-term accumulation of the metabolite "M670H05", but the extent of accumulation is not known. Thus, long-term exposure of plants or animals cannot be assessed at this time. Likewise, if time-dependent binding to soils rather than biotransformation control the "disappearance" of topramezone in soils, there is a potential for carryover from season-to-season. Because the rate of adsorption/desorption of topramezone to soils is not known, the bioavailability of topramezone via desorption cannot be assessed.

c. There are no terrestrial plant data to evaluate the phytotoxicity of the metabolites of topramezone. Metabolite "M670H05" has the potential to accumulate in soils from carryover. The effect of this metabolite on plants is not known.

d. Even though the water-sediment studies have deficiencies that must be addressed by the registrant, two different metabolites may be present in water-sediment systems (M670H01 under aerobic conditions and M670H10 under anaerobic conditions). The metabolites M670H01 and M670H10 have molecular structure features required for herbicides that exhibit the same mode of action as topramezone, isoxaflutole, and mesotrione. Potentially these two metabolites may also have herbicidal effects, but there are no plant data to show if they are herbicide active or not.

e. Topramezone is a carotenoid biosynthesis inhibitor (via inhibition of an enzyme, 4-HPPD). The effect of topramezone on non-target plants at the carotenoid pigment development stage is not known. Current plant studies do not address effects at higher levels of development. Therefore, there is a potential for inhibition of carotenoid biosynthesis in non-target plants at higher developmental stages such as prior to flowering, fruit-development and maturing.

II. Problem Formulation

A. Stressor Source and Distribution

1. Source and Intensity

Topramezone (BAS 670H) is a new active ingredient proposed as a selective, systemic, post-emergence herbicide for weed control on grain corn, popcorn, seed corn, and sweet corn. It may be used on conventional and herbicide resistant/tolerant hybrids for field corn. The proposed end-use product is 'BAS 670 H 336 SC", a soluble concentrate formulation containing 29.7% topramezone. The proposed label allows ground and aerial applications, but application through irrigation systems are not allowed. The maximum application rate per growing season is 0.022 lbs ai/acre (25 g/ha).

Corn cultivation in the United States is extensive. Thus, a wide range of soils, climates, hydrological characteristics, and agricultural practices are expected throughout the corn growing areas. Therefore, the use of topramezone is likely to encompass a wide variety of ecosystems. As a herbicide, adverse effects to non-target plants can be anticipated. Topramezone may reach non target sites by spray drift and/or runoff from adjacent agricultural sites.

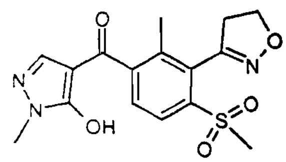
2 Chemical Identity of the Stressor

Topramezone (BAS 670H) is a new herbicide active ingredient belonging to the phenylpyrazolyl ketone chemical family of herbicides[1] Refer to Table II.1 for further chemical identity information.

Table II.1 Chemical Identity of the Stressor

Type of Information	Chemical Specific Information
Common Name Company Code	**Topramezone** BAS 670H
CAS Registry Number	210631-68-8
CAS Name	[3-(4,5-Dihydro-3-isoxazolyl)-2-methyl-4-(methylsulfonyl)phenyl](5-hydroxy-1-methyl-1H-pyrazol-4-yl) methanone
IUPAC NAme	[3-(4,5-dihydro-isoxazol-3-yl)-4-methylsulfonyl-2-methylphenyl]-(5-hydroxy-1-methyl-1*H*-pyrazol-4-yl)methanone
OPP Name and Code	[3-(4,5-Dihydro-3-isoxazol-3-yl)-4-methanesulfonyl-2-methyl-phenyl](5-hydroxy-1-methyl-1H-pyrazol-4-yl) methanone 123009
Empirical Formula	C16H17N3O5S

[1] Other members of this family include benzofenap, pyrazolynate, and pyrazoxyfen

Type of Information	Chemical Specific Information
Molecular Weight	363.39 g/mol
Molecular Structure	
Proposed Name of End-use Product	"BAS 670 336SC Post-emergent Corn Herbicide" (29.7% topramezone)

a. Physical and Chemical Properties

Physical and chemical properties are intrinsic properties of a chemical. Some of these properties can be use to identify potential behavior of a chemical in the environment. For example, a low vapor pressure and Henry's Law Constant suggest low potential for volatilization from soil and water. The physical and chemical properties of topramezone are presented in Table II.2.

Table II.2 Physical and Chemical Properties of Topramezone

Parameter	Value	
Solubility in Water (20°)	pH	gL-1
	3	0.06
	5	0.98
	7	15
	9	23.4
Solubility in Non-aqueous Solvents, g/100 mL at 20°C	Solvent	Solubility
	Acetone	<1.0
	Acetonitrile	<1.0
	Dichloromethane	2.5 - 2.9
	Ethyl acetate	<1.0
	Methanol	<1.0
	N-heptane	<1.0
	N,N-dimethylformamide	11.4-13.3
	1-octanol	<1.0
	Olive oil	<1.0
	2-propanol	<1.0
	Toluene	<1.0
Dissociation constant (pKa)		4.06
Vapor Pressure, (25°)		1×10^{-10} Pa (Measured) 1.3×10^{-10} Pa (Estimated by EPI)
Henry's Law Constant (25°)		3×10^{-15} Pa-m3mole-1 (Estimated by EPIWIN 3.1)

Parameter	Value	
Log *n*-octanol/water Partition Coefficient (Log Kow) at 20°C	Buffer pH 4 7 9	Log Kow – 0.81 – 1.52 – 2.34
UV/visible absorption spectrum (pH not specified) (where ϵ is the molar absorption coefficient)	λ, nm 207 272 300 410	ϵ, $mol^{-1}cm^{-1}$ 27 077 8601 5800 410
Other	Topramezone is a white solid with a density of 1.425 gcm^{-3} and a Melting Point range of 220.9 to 222.2° C	

Topramezone is a weak acid (pKa 4.06; 1:1 ratio of anionic form to undissociated acid). Thus, in the environmentally significant pH range of 5 to 9, topramezone is not likely to predominate as the undissociated species. The concentration of dissociated topramezone will increase with increasing pH. However, at pHs near the pKa, some undissociated topramezone can still be present. In general, anions do not tend to bind to soils/sediments[2] and therefore, based on the value of the pKa alone, topramezone is expected to partition predominantly into the water column and to be mobile.

Based on the vapor pressure alone, topramezone has low potential to volatilize from soils. The low Henry's Law Constant (estimated) and the high, pH-dependent solubility of topramezone suggest that topramezone has a low potential to volatilize from water. The very low, pH dependent *n*-octanol/water partition coefficients indicate that topramezone has a very low potential to bioaccumulate in fish.

Topramezone absorbs energy (i.e., has electronic absorption bands) within the spectrum of sunlight. Thus, it meets the necessary condition to undergo direct photolysis in water. However, this necessary condition alone can not be used to conclude that it will actually photolyze, as the absorbed energy must be sufficient to cause bond breaking, rearrangements, or photoredox reactions. Therefore, the results of the photolysis in water study must be used to assess the effect of sunlight on topramezone.

b. Environmental Fate Parameters

Environmental fate parameters are taken from the environmental fate studies required to support registration of a pesticide. Unlike the intrinsic, physical and chemical properties, environmental fate parameters are extrinsic properties that are specific to the test media and conditions of the studies (e.g., type of soil, temperature, moisture content). Therefore, some information about

[2] Unless other biding mechanisms , such as chemisorption and hydrogen bonding are involved.

these conditions have been included in Table II.3.

Table II.3 Environmental Fate Parameters for Topramezone

Environmental Studies	Half-life (Linear)	Experimental Conditions	Comments
161-1 Abiotic Hydrolysis	Could not be established-Stable	pH 5, 7, and 9, 25° C	Topramezone is a weak acid (pKa 4.06). The solubility and concentration of the anionic form increases with increasing pH
161-2 [Direct] Photolysis	132 days based on a 12 hrs light/dark cycle	Artificial xenon-arc lamp, mimicking spring sunlight at 40° latitude North 22° C	Even though topramezone absorbs energy within the wavelength range of sunlight, the observed photoreaction quantum yield (ϕ) is very low. Thus, direct photolysis in water under environmental conditions is not a significant degradation route
161-3 Photolysis on Soil	> 33 days	Artificial xenon-arc lamp, mimicking spring sunlight at 40° latitude North Sandy loam soil 22° C	Photolysis on soil under environmental conditions is not a significant degradation route
162-1 Aerobic Soil Metabolism: Topramezone (6 soils) Metabolite M670H05 (NC sandy loam)	125 to > 1 year 55 to > 1 year	Topramezone Studies were conducted in the following soils: loam (Idaho), silt loam (Indiana), loam (Iowa), clay (Minnesota), silt loam (South Dakota) and sandy loam (North Carolina) Studies with topramezone an M670H05 were conducted at 27° C	Nature and relative ratio of biotransformation products, including CO_2, varied across the soils The most frequently identified metabolite was M670H05. Only in one soil "M670H01" was identified at >10% of the applied radioactivity
162-3 Anaerobic Aquatic	13 to 24 days (total system) Deficiencies need to be addressed by registrant	Lake reservoir in South Dakota; silt loam sediment 25° C	Only metabolite was M670H10, which is structurally very different from other metabolites. This metabolite is consistent with what is expected in a reducing (anoxic) environment.

Environmental Studies	Half-life (Linear)	Experimental Conditions	Comments
162-4 Aerobic Aquatic	System 1: > 120 days (water, sediment, and total system) System 2: Water: 11 days; Sediment: 49- 78 days Whole system: 19 to 24 days	System 1: River water; loamy sand sediment System 2: Pond water; loam sediment 20° C	Marked differences were observed in the properties of water of the two systems. Which property (or properties) of the pond water control the persistence of topramezone in not known.
163-1 Mobility in soil (Batch-equilibrium adsorption/desorption)	Kads (Freundlich): 1.4 to 4.9 Koc: 38 to 303	Same soils as those used in the aerobic soil metabolism study	Topramezone is a weak acid (pKa 4.06). Thus, the concentration of the anionic form increases with increasing pH. The higher the concentration of the anionic form, the weakest the binding to soils. However, the pH range of the soils was too narrow to adequately correlate mobility with pH

Note: The hydrolysis, direct aqueous photolysis, photolysis on soil, aerobic soil metabolism, and batch-equilibrium adsorption/desorption studies are acceptable. The biotransformation of topramezone in water-sediment systems (anaerobic and aerobic) may be acceptable if satisfactory additional information is received from the petitioner.

From the data summarized in Table II.3 biotransformation could be identified as a route of transformation of topramezone in the environment and considerable variability in persistence and metabolites might be expected across the use areas of this herbicide. However, time-dependent sorption, as evidenced from the increase of non-extractable residues in soils/sediment with time, might be an important dissipation route for topramezone.

3. Pesticide Type, Class, and Mode of Action

Topramezone belongs to the phenyl pyrazolyl ketone chemical family of herbicides. It is a selective, systemic herbicide proposed for post-emergence control of broadleaf and grass weeds on corn.

The mode of action of topramezone is inhibition of carotenoid biosynthesis by inhibiting the 4-hydroxyphenyl-pyruvate-dioxygenase enzyme (4-HPPD)[3] in the chlorophyll pathway and

[3] See http://www.plantprotection.org/HRAC/MOA.html

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ultimate breakdown of chloroplast. Inhibition of carotenoid[4] biosynthesis causes **"albino growth"** in new plant tissues. Topramezone is absorbed by the leaves, roots and shoots, then translocated to the growing points of the sensitive weeds. This causes a strong bleaching activity on the growing zones of the shoots within 2-5 days of application. Plant growth does continue for a time, but without production of green photosynthetic tissue, growth of affected plants can not be maintained. Even though topramezone do not directly inhibit chlorophyll biosynthesis, direct exposure to light (photooxidation) causes plant death within 14 days after application. Carotenoids are also present in some bird feathers (e.g, flamingo; canary) and some crustaceans. The 4-HPPD enzyme also occurs in mammals and is involved in tyrosine catabolism.

Topramezone shares the same mode of action with isoxaflutole (cyclopropylisoxazole family of herbicides) and mesotrione (a triketone belonging to the benzoylcyclohexanedione family) . The common structural features associated with 4-HPPD inhibition by these herbicides are: (1) at least one carbonyl (keto) group must be a substituted benzoyl group[5] and (2) at least a keto group is able to enolise (i.e., keto-enol tautomerism that favors the enolate tautomer). It is the enolate that is capable of inhibiting the enzyme by a competitive reaction of the enolate with dioxygen (molecular oxygen) at the Fe(II) site of the enzyme. This Fe (II) is the reaction site of the enzyme. The Fe(II) in 4-HPPD is a non-heme Fe(II)[6]. Inhibition of the enzyme by the enolate involves Fe-

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4 Carotenoids are red, yellow and orange pigments that are widely distributed in nature. Although specific carotenoids have been identified in photosynthetic centers in plants, bird feathers, crustaceans and marigold petals, they are especially abundant in yellow-orange fruits and vegetables and dark green, leafy vegetables.

Carotenoids are a class of hydrocarbons (carotenes) and their oxygenated derivatives (xanthophylls) consisting of eight isoprenoid units joined in such a manner that the arrangement of isoprenoid units is reversed at the centre of the molecule so that the two central methyl groups are in a 1,6-positional relationship and the remaining nonterminal methyl groups are in a 1,5-positional relationship. All carotenoids may be formally derived from the acyclic structure of $C_{40}H_{56}$ having a long central chain of conjugated double bonds, by (i) hydrogenation. (ii) dehydrogenation, (iii) cyclization, or (iv) oxidation. or any c combination of these processes

http://www.chem.qmul.ac.uk/iupac/carot/car1t7.html

5 [2-(methylsulfonyl)-4-trifluoromethylphenyl]- in isoxaflutole, [4-(methylsulfonyl)-2-nitrobenzoyl]- in mesotrione, and [3-(4,5-dihydro-3-isoxazolyl)-2-methyl-4-(methyl-sulfonyl)phenyl] in topramezone.

6 Zhu, Y-Q, et al. 2005. *The Synthesis and Herbicidal Activity of 1-Alkyl-3-(α-hydroxy-substituted benzylidene)pyrrolidine-2,4-diones*. **Molecules**, 10: 427-434.

Wu, SC, et al. 2002. *Mode of action of 4-hydroxyphenylpyruvate dioxygenase inhibition by triketone-type inhibitors*. **J. Med. Chem.**, 23, 45(11), pp. 2222-8.

Continuation of Footnote 6

Matriange, M. et al. 2005. *p-Hydroxyphenylpyruvate dioxygenase inhibitor resistant plants*. **Pest Manag Sci.** 61(3): 269-76 .

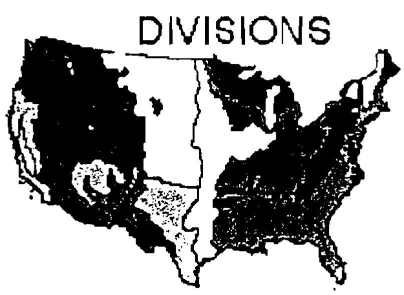
Yan, C, et al. 2004. *Structural basis for herbicidal inhibitor selectivity revealed by comparison of crystal structures of plant and mammalian hydroxyphenylpyruvate dioxygenases*. **Biochemistry**, 43(32): 10414-23.

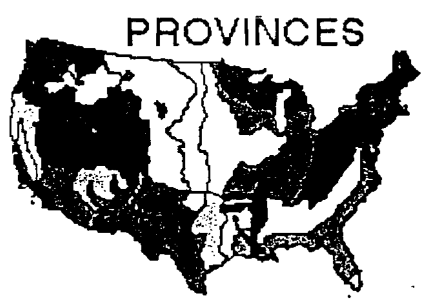
Meazza, G., et al. 2002 *The inhibitory activity of natural products on plant p-hydroxyphenyl-pyruvate dioxygenase* . **Phytochemistry**, 60(3): 282-8.

enolate chelation[7], which causes a reduction of the activity of 4-HPPD as a dioxygenase. That is, it inhibits the incorporation of both oxygen atoms of dioxygen needed to form homogentisate[8], a precursor for pigment biosynthesis[9]. This mechanism of inhibition also applies to animal 4-HPPD by decreasing the formation of homogentisate, a degradation product of tyrosine.

4. Overview of Pesticide Usage

As a new herbicide, the extent at which topramezone will be actually used cannot be anticipated. However, it is reasonable to assume that it will be used in major corn growing areas of field, popcorn, and sweet corn (See Figure II.1). Therefore, use of topramezone may be widespread and will expand throughout different ecoregions of North America[10] and compare to corn acreage planted in the United States (Figure II.1)





Continuation Footnote 7,

Simkin, A.J., et al. 2003. *Comparison of carotenoid content, gene expression and enzyme levels in tomato (Lycopersicon esculentum) leaves.* **Z. Naturforsch. [C]**, 58 (5-6): 371-80.

Corona, V., et al. 1996. *Regulation of a carotenoid biosynthesis gene promoter during pigment development.* **Plant J.** 9(4): 505-12.

[7] From a close inspection of the molecular structure of topramezone, isoxaflutole, and mesotrione the keto-oxygen can be identified as the binding atom.

[8] Biosyntehesis of homogentisate includes a decarboxylation effect and rearrangement of the pyruvate side chain.

[9] Prescott, A.J. and Lloyd, M.D. 2000. *The Fe(II) and 2-oxoacid-dependent dioxygenases and their role in metabolism.* **Nat. Prod. Rep.**, 17, 367-383.

Bassam, A., Borowski, and Sieghbahn, P.E.M. 2004. *Quantum chemical studies of dioxygen activation by mononuclear non-heme iron enzymes with the 2-His-1-carboxylate facial triad.* **Dalton Trans.**, 3153- 3162.

Sailland, S.L., et al. 1999. *Crystal structure of Pseudonomas fluorescens 4-hydroxyphenyl-pyruvate dioxygenation in the tyrosine degradation pathway.* **Structure Fold Des**, 7(8), 977-88.

[10] http://www.fs.fed.us/land/ecosysmgmt/ecoreg1_home.html

The Bailey's classification system is comprised of broad "Domains"(not shown). Each "Domain" is then narrowed down into "Divisions" and each "Division" is further divided into "Provinces" The continental USA (conterminous states) is comprised of three Domains: a Dry Domain (center), a Humid Temperate Domain (East and West of the Dry Domain), and a Humid Tropical Domain (Southern Florida). There are 7 Divisions in the Dry Domain, 11 in the Humid Temperate Domain, and 1 in the Humid Tropical Domain.

A brief description of selected provinces where corn is grown is presented below in an attempt to show the variability in soils and climate among corn growing areas.

Everglades Province (Southern Florida); Savanna Division:
Almost flat marl and limestone shelf generally covered with a few feet of muck and a little sand. Elevation ranges from sea level to 25 ft (7.6 m). Average annual temperatures in this tropical climate range from 70 to 75F (21 to 24C), with minimums from October to February. Wet season between late spring and middle of fall and dry season between late fall and early spring. Histosols are the principal soils. In slightly less wet parts of the southern Everglades, Inceptisols occupy extensive areas Sweet corn is cultivated in this area.

Outer Costal Plain Mixed Forest; Subtropical Division (Brown: Eastern USA)

This province comprises the flat and irregular Atlantic and Gulf Coastal Plains down to the sea. The climate regime is equable, with a small to moderate annual temperature range. Average annual temperature is 60 to 70F (16 to 21C). Rainfall is abundant and well distributed throughout the year.

Soils are mainly Ultisols, Spodosols, and Entisols

Prairie Parkland Temperate Province; Prairie Division (Yellow)

It covers an extensive area from Canada to Oklahoma, with alternating prairie and deciduous forest. Summers are usually hot, and winters are cold, especially in the northern part of the province. Average annual temperatures may reach 40F (4C) in the north and 60F (16C) in the south. Winters are short and relatively mild in southerly areas. The frost-free season ranges from 120 days along the northern fringe to 235 days in the south. Average annual precipitation ranges from 20 to 40 in (510 to 1,020 mm), falling mainly during the growing season.

Mollisols dominate throughout the province. Alfisols are found in the Mississippi Valley

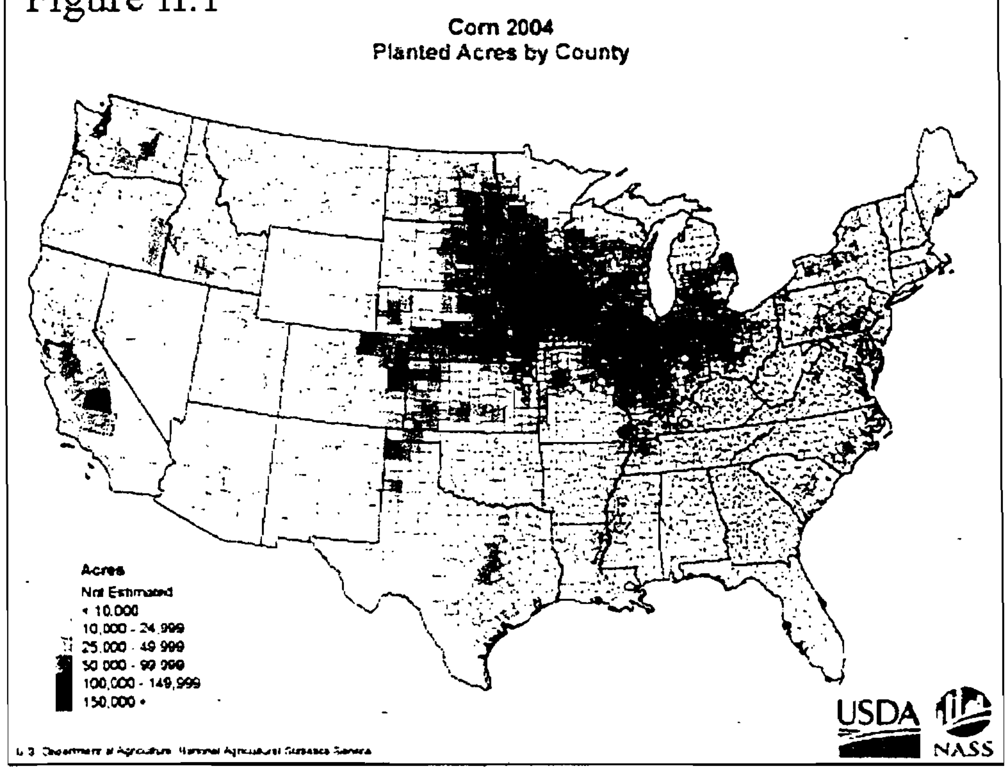
Southeastern Mixed Forest; Subtropical Division (Pink, Southeastern USA)

The climate is roughly uniform throughout the region. Mild winters and hot, humid summers are the rule; the average annual temperature is 60 to 70F (15 to 21C). The growing season is long (200 to 300 days), but frost occurs nearly every winter. Precipitation, which averages from 40 to 60 in (1,020 to 1,530 mm) annually, is rather evenly distributed throughout the year, but peaks slightly in midsummer or early spring, when it falls mostly during thunderstorms. Precipitation 18 exceeds evaporation, but summer droughts occur. Snow falls rarely and melts almost immediately

Ultisols dominate throughout the region, with locally conspicuous Vertisols formed from marls or soft limestones. The Vertisols are clayey soils that form wide, deep cracks when dry.

Inceptisols on floodplains of the major streams are among the better soils for crops

Figure II.1



http://www.usda.gov/nass/graphics/county04/pages/CR-PL0TRGBChor_gif.htm

The maximum proposed application rate is 0.022 lb ai/acre (25 g/ha) per growing season. is. It may be applied in 2 split applications not to exceed the seasonal total maximum of 0.022 lb ai/acre, allowing 7 days between sequential application. Aerial and ground applications are proposed, but application through irrigation systems are not allowed. As a post-emergence herbicide, it will be applied when weeds are actively growing. The product may be used in conservation tillage as well as conventional tillage production systems.

Topramezone needs to be applied in conjunction with a nitrogen fertilizer and a petroleum -based or vegetable- seed based oil concentrate or a methylated seed oil as adjuvant. It may be mixed with other recommended herbicides, but should not be mixed with isoxaflutole or mesotrione. Topramezone can be applied up to 45 days prior to corn harvest Therefore, time of application is expected to vary depending on the typical harvest period for different use areas and type of corn crop.

5. Receptors

1. Aquatic Effects

For the aquatic ecosystem, ecological receptors include all aquatic life (fish, amphibians, invertebrates, plants) and those terrestrial animals (e.g., birds and mammals) that consume aquatic organisms. Based on the above sources/transport pathways, exposure media, and potential receptors of concern, specific questions or risk hypotheses formulated to characterize direct effects of topramezone application to selected assessment endpoints is provided below.

Risk to aquatic animals are based on registrant submitted acute and sublethal laboratory tests with aquatic vertebrates (Rainbow trout, Bluegill sunfish and Sheepshead minnow) and invertebrates (Water fleas, Mysid shrimps and Eastern oysters) Risk to aquatic vascular and nonvascular plants will be based on registrant submitted short-term tests to algae and diatoms, and duckweed.

2. Terrestrial Effects

Ecological receptors of concern identified for consideration in the terrestrial environment include primary producers, represented by both upland and wetland/riparian vegetation, and primary and secondary consumers, both vertebrates and invertebrates, representing common ecological functional feeding groups (*i.e.*, herbivores and insectivores). Herbivores as used here include animals that feed on foliage (stems and leaves), seeds, and/or fruit; the term granivore is sometimes used to identify animals that feed primarily on seeds. Omnivores (*i.e.*, consumers that feed on a mixed diet of animals and plants) are also potentially exposed but are not specifically included in the receptor list for a screening level risk assessment because exposure concentrations and risk levels will fall between the exclusive feeding groups.

Based on the sources/transport pathways, exposure media, and potential receptors of concern, specific questions or risk hypotheses formulated to characterize direct effects of topramezone following application on areas to selected assessment endpoints is provided below.

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Risk to terrestrial animals will be based on registrant submitted acute and reproductive laboratory tests with birds (Northern bobwhite quail and mallard duck) and mammals (Norway rat or house mouse). to represent all terrestrial vertebrates. Risk to terrestrial plants will be assessed using registrant submitted vegetative vigor and seedling emergence laboratory tests with 10 species of crops (six dicots: soybean, cabbage, lettuce, radish, tomato and bean; four monocots: ryegrass, onion, wheat, and corn).

3. Ecosystems at Risk

The terrestrial ecosystems potentially at risk include the treated area and areas immediately adjacent to the treated area that might receive drift or runoff, and might include other cultivated fields, fence rows and hedgerows, meadows, fallow fields or grasslands, woodlands, riparian habitats and other uncultivated areas. For Tier 1 assessment purposes, risk will be assessed to terrestrial animals assumed to exclusively occur in the treated area. Risk will be assessed to terrestrial plants assumed to exclusively occur in areas immediately adjacent to, and in wetlands receiving runoff from treated areas.

Aquatic ecosystems potentially at risk include water bodies adjacent to, or down stream from the treated field and might include impounded bodies such as ponds, lakes and reservoirs, or flowing waterways such as streams or rivers. For uses in coastal areas, aquatic habitat also includes marine ecosystems including estuaries. For Tier 1 assessment purposes, risk will be assessed to aquatic animals and plants assumed to occur in small, static ponds receiving runoff and drift from treated areas.

As a new chemical, the use areas of topramezone are not known, but it is reasonable to assume that it may be used in major corn growing areas. However, corn cultivation in the United States is very widespread and includes a wide range of soils, climates, altitude, hydrology, and weather patterns that can support different and distinct ecosystems. For example, corn grown in the Mid-Atlantic states or Florida may be close to wetlands and marine ecosystems while corn grown and/or fields draining along the Mississippi basin would be predominantly freshwater ecosystems. It should be noted that Florida is a major grower of sweet corn and that the sweet corn growing areas are predominantly located in counties around the Everglades.

Because corn is grown practically within all latitudes of the country, planting times, times of weed emergence, growing season , and harvest times can vary considerably from region to region. Even for corn grown in the same area, differences in use scenarios can be expected when corn is grown as "sweet corn" (a warm weather crop) or as "field corn", given that the intervals between planting and harvesting are shorter for sweet corn than for field corn.

C. Assessment Endpoints

Environmental Fate Assessment

Laboratory scale and field studies serve to identify the most important routes of dissipation of a chemical stressor under environmental conditions. It is important to recognize that the studies are conducted on a limited number of test systems (soils; water-sediment systems), experimental conditions, and field sites. Therefore, environmental fate and exposure assessments are limited by guideline design and number of test systems, which may not be representative for all of the potential use areas of a pesticide.

Four major components enter in any environmental fate assessment of a chemical:

1. Kinetics- Identification of how fast and in which media the chemical dissipates (i.e., the persistence of the chemical)
2. Transformation- Identification of processes (abiotic and microorganism mediated) involved in the degradation of the chemical in different environmental media, the nature of the transformation products, and molecular features that may suggest potential herbicidal effects of these products.
3. Transport- Identification of the potential movement of the chemical (or transformation products) in the different environmental compartments
4. Accumulation- Identification of the potential of a chemical (or transformation products) to accumulate in soils and/or sediments or to bioaccumulate in organisms.

Ecological Toxicity Assessment Endpoints

The measurement endpoints addressed in this assessment include survival, growth, and reproduction of individual terrestrial and aquatic animals and by inference, health of populations and communities. Effects to terrestrial animals are assessed by considering the potential for survival and reproductive risk to birds and mammals. These effects seen in birds are intended to also represent potential risk to reptiles.

Effects to aquatic animal communities are assessed by considering potential for survival risk to individual freshwater and estuarine/marine fish and invertebrates, sub-lethal effects to fish and reproductive effect to freshwater invertebrates. The assessment cannot address potential for reproductive risk to a broad range of aquatic animals because reproductive toxicity tests are only available for invertebrates. Therefore, there is uncertainty in the potential for adverse effects to aquatic communities (except invertebrates) through potential reproductive effects. The fish early life stage study results compared to aquatic EECs suggests low sub-lethal risk, but that study does not address reproductive endpoints.

Effects to aquatic plant communities is assessed by analyzing the potential risk to growth of vascular and nonvascular populations. Effects to terrestrial plant communities is determined by assessing potential growth and survival of individual plants.

Generally, for either terrestrial or aquatic ecosystems, if a screening level assessment using upper bound exposure levels in conjunction with the most sensitive toxicity values result in a presumption of minimal risk at the individual level, that is, no LOCs are exceeded, there is a substantial degree of certainty of minimal impacts to populations or communities. A presumption of risk at the individual level *could* indicate a population or community effect. Refinement of the risk conclusions would be then needed to draw reasonable conclusions regarding the potential for population or community effects from the screening level assessment.

Specific toxicity endpoints required and used for ecological assessment of topramezone are listed below. A detailed characterization of the rationale for the use of these endpoints may be found in "Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs" (http://www.epa.gov/espp/consultation/ecorisk-overview.pdf)

D. Conceptual Model

1. Risk Hypotheses

Risk hypotheses are specific assumptions about potential adverse effects (i.e., changes in assessment endpoints) and may be based on theory and logic, empirical data, mathematical models, or probability models (EPA, 1998). For this assessment, the risk is stressor-linked, where the stressor is the release of topramezone to the environment via aerial or ground applications to corn The following risk hypothesis is presumed for this screening level assessment:

Topramezone has the potential to runoff from soils (high mobility and persistence) and/or enter surface water or non-target fields by spray drift. Thus, topramezone has the potential to affect the food-web of the non-target aquatic and terrestrial ecosystems and cause reduced survival, and reproductive and/or growth impairment for both aquatic and terrestrial animal and plant species. Furthermore, topramezone inhibits the biosynthesis of carotenoids, which could result in discoloration of plants that are attractive to animals as food source. This last point is mentioned as a possible effects, but is not specifically assessed in this document.

2. Conceptual Model Diagram

A generalized, conceptual model for topramezone is shown in Figure II.2

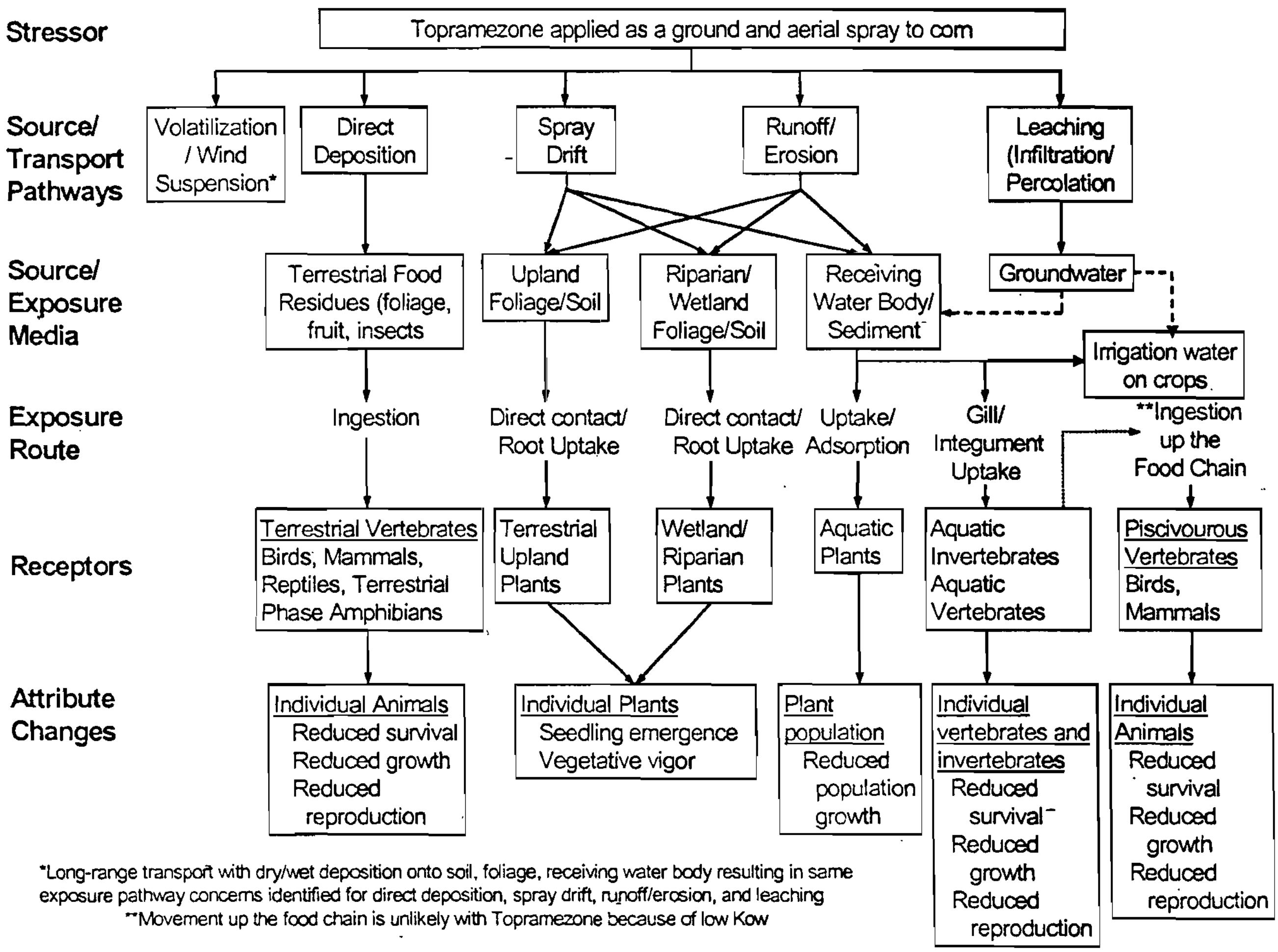

Figure II.2 Conceptual Model for Exposure Routes for Topramezone Herbicide

This generalized conceptual model diagram (Figure II.2) does not include exposure to transformation products or other dissipation processes that are specific to topramezone. A preliminary environmental fate assessment indicated that transformation of topramezone in the environment is controlled by microorganisms (i.e., biotransformation). However, this preliminary assessment also suggested that time-dependent sorption may be controlling the overall dissipation of topramezone in soils and/or sediments as a competitive process with biotransformation.

The chemical species to which animal and plants may be exposed, in which media, and the route of exposure are summarized below. All of these chemical species were considered in the exposure assessment, at least qualitatively.

Potential Exposure of Topramezone and Metabolites in Ecosystems.

Chemical Species	Observed	Route of Exposure	Exposure
Topramezone	All studies (Test substance)	Direct application to treated field Spray drift Runoff	Terrestrial Aquatic
"M670H05"	Aerobic Soils	Formation in the treated field Runoff	Terrestrial (as high as 16%) Aquatic
"M670H01"	Some aerobic soils Aerobic water-sediment system	Formation in the treated field Runoff Formation in aerobic water-sediments	Terrestrial (10%) Aquatic (10%)
"M670H10"	Anaerobic water-sediments	Formation in anaerobic water-sediments	Aquatic (16% water)

Of these metabolites, "M670H01" and "M670H10" have molecular features that suggest that they may potentially exhibit herbicidal activity, but no plant toxicity data or other ecological toxicity data are available for these metabolites.

E. Analysis Plan

1. Preliminary Identification of Data Gaps and Methods

As the first step in the analysis plan, environmental fate and toxicity studies were evaluated for completeness of data required under FIFRA and the scientific validity of the submitted studies. Data from these studies were taken to gather the necessary information to assess the exposure and effects of topramezone when used as a post-emergence herbicide on corn.

The assessment was performed at the screening level only, assuming that potential use of topramezone would be in any corn growing areas (field corn, seed corn, popcorn, and sweet corn).

Environmental Fate

All of the environmental fate studies required under FIFRA for registration of a terrestrial food-use herbicide were submitted by the petitioner. Although some of the studies have deficiencies that introduce a high level of uncertainty into certain aspects of the assessment, it was deemed in general that data from the studies was sufficient to generate a screening exposure assessment for topramezone. That is, to identify persistence, degradation pathways, transformation products, transport mechanisms (topramezone and products), and the potential to accumulate on soils, sediments, or fish. These data served as the basis for selecting the appropriate environmental fate input parameters for use in simulation to estimate exposure in ecosystems potentially at risk models.

Among the major uncertainties brought out from the laboratory studies are:

(a) The behavior of topramezone in water-sediment systems (anaerobic; aerobic) because of study deficiencies and/or inadequacy of some of the water-systems.

(b) The pH-dependence of adsorption of the weak acids topramezone and its soil metabolite M670H05 onto soils (and hence, mobility) could not be adequately established because of the narrow pH range of the studies.

(c) The potential for carryover from one treatment season to the next of the aerobic soil metabolite M670H05 was identified, but it could not be adequately assessed because no aerobic soil metabolism data were available beyond 1 year post-application that would indicate that the amount of this metabolite keeps increasing.

(d) The potential competition between rate of adsorption and biotransformation in the overall dissipation of topramezone in soils and sediments. It was observed that levels of non-extractable residues increased with time[11], but the role of the rate of adsorption (time-dependent sorption; kinetics of sorption) is not known because studies on the kinetics of sorption are not required under current guidelines.

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[11] Recent research with chlorsulfuron and metsulfuron suggests that the herbicide stays associated with the fulvic fraction of the soil from which is then slowly released;

Gao. J. and Sun, J. 2002..*Studies on bound 14C-chlorsulfuron residues in soil.* **J. Agri. Food Chem.** 50 (8), pp 2278-82.

Ye, Q., Sun, J., and Wu, J. 2003. *Causes ofphytotoxicity of metsulfuron-methyl bound residues in soil.* **Environ. Pollut.,** 126 (3), 417-23.

Non-extractable residues of topramezone were also predominantly associated with the fulvic acid fraction. Although topramezone is not a sulfonylurea herbicide, it is feasible that topramezone may exhibit a similar behavior. This topic is further discussed under the "Risk Description" section.

Terrestrial field dissipation studies were conducted in Indiana, South Dakota, California, and Ontario (Canada). While the selected sites include areas where corn is grown, the Mid-Atlantic and Southeastern states were not represented despite the fact that sweet corn may be extensively grown in those regions. Thus, the behavior of topramezone in those areas is not known. However, a Florida (sweet corn) and East North Carolina corn scenarios were included among the standard scenarios selected for calculating EECs in aquatic systems.

Ecological Toxicity

All of the ecological studies required under FIFRA for registration of a terrestrial food-use herbicide were submitted by the petitioner. Although some of the studies have deficiencies that introduce a level of uncertainty into the assessment, it was satisfactory in general that data from the studies was sufficient to generate a screening ecological assessment for topramezone.

Among the uncertainties flagged in the assessment from the laboratory studies are:

(a) The NOAEC value in the mallard duck reproduction study is in question because statistically significant reductions in growth to chicks occurred and adult animals lost weight at all treatment levels.

(b) Data verifying the stability of the test substance in treated feed of the avian studies were not provided.

(c) The toxicity to aquatic vascular plant was based on only one species, *Lemna gibba*, which is a monocot tested as a surrogate representing vascular plants. It is not possible to distinguish the toxicity between aquatic dicots or monocots based on the only species tested.

(d) Toxicity effects to freshwater diatoms is unknown. In the study conducted with *N. pelliculosa*, the observed effects could not be distinguished between pH effects and topramezone effects. Thus, it cannot be ruled out that undissociated topramezone may be more toxic than the anionic form (i.e., that the phytotoxicity of topramezone increases with increasing pH). Because the study was not performed at the pH recommended levels in the guideline, it is classified as invalid.

(e) Dry weight was not measured in the aquatic invertebrate life cycle with daphnids. It is unknown if topramezone effects growth to invertebrates.

(f) Terrestrial plant toxicity tests were not tested with the metabolite M670H05 or other metabolites. In consideration of crop rotations, there is a potential for M670H05 to accumulate in soils from carryover. It is unknown if crops planted in previously corn fields treated with topramezone will be impacted from the metabolite.

(g) No estuarine/marine fish early life-stage toxicity test was conducted for topramezone. The NOAEC value for estuarine/marine fish was derived from the freshwater fish early life stage based on the assumption that both fish are of equal sensitivity.

2. Measures to Evaluate Risk Hypotheses and Conceptual Model

1. Measures of Exposure

Topramezone is a post-emergence herbicide that would be applied to corn at very low rates (maximum of 0.022 lbs a.i./acre; 25 g/ha, per growing season). Thus, effects to the growth of plants at low levels of exposure was identified as a potential, major concern.

Therefore, to estimate environmental concentrations in aquatic ecosystems, the Tier II simulation models PRZM (Version 3.12) and EXAMS were used on ten different standard corn scenarios. As a new chemical, monitoring data for topramezone is non-existent. Therefore, such data cannot be incorporated into the assessment.

Exposure to birds and mammals feeding on a treated field was estimated using the Terrestrial Residue EXposure (TREX) simulation model. Exposure to plants was estimated using the "TerrPlant" and AgDrift models

2. Measures of Effect

The toxicity data that will be used to address the assessment endpoints identified above are listed below.

Avian and Mammalian, Survival of Individuals

To determine potential for survival of birds from direct ingestion of sprayed vegetative matter, the avian LC50 value was used. For mammals, risk to individual survival was assessed using the mammalian LD50.

Avian and Mammalian Reproduction:

Potential risk to reproduction and growth of birds that forage on vegetation, seeds, and insects contaminated with topramezone residues during the breeding season are assessed by using the avian reproduction NOAEC. Potential risk to reproduction and growth of mammals that forage on vegetation, seeds, and insects with topramezone residues during the breeding season are assessed by using the mammalian reproduction NOAEC.

Toxicity to Terrestrial Non-Target Plants:

Potential risk to growth and survival of terrestrial plants is assessed by estimating exposure to dryland and semi-aquatic areas receiving drift and runoff from treated sites and comparing this exposure to the EC25 and NOAEC for the dicot and monocot. The EC25 is used to assess risk to non-endangered species; the NOAEC is used to assess risk to endangered species of terrestrial plants.

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Freshwater and Estuarine/Marine Fish and Invertebrates

Potential risk to survival of freshwater fish and invertebrates in static water bodies exposed via runoff and drift is assessed using the fish 96-hour LC50 and the aquatic invertebrate 48-hour EC50.

Potential risk to growth and survival of fish from longer exposure is assessed using the early life-stage test NOAEC, which determines effects from egg hatch through early stages of development. For invertebrates, risk to reproduction, survival and growth is assessed using the life cycle NOAEC.

Toxicity to Aquatic Plants

Potential risk to growth and populations of aquatic plants is assessed using the EC50s and NOAECs for aquatic vascular and nonvascular plants. The EC50s are used to assess risk to non-endangered aquatic plants, the NOAEC or EC05[12] is used to assess risk to endangered aquatic plants.

3. Measures of Ecosystem and Receptor Characteristics

Topramezone is proposed as a herbicide to control emerged broadleaf and grassy weeds. The time of application depends on the developmental stage of the specific weed. Corn is cultivated extensively throughout the United States. Thus, planting, weed development, crop maturity, and harvesting times can vary widely across corn growing regions as well as between uses on field corn or on sweet corn. Because the timing of application needs to be considered together with the developmental stage of non-target organisms for representative, potential use sites, ten standard corn scenarios were considered to estimate environmental concentrations of topramezone in aquatic ecosystems. Each of the different scenarios used in PRZM and EXAMS consider soil characteristics selection of multiple , latitude, weather patterns, and agricultural practices (e.g., , planting times, times of weed emergence, growing season , and harvest times) to account for variability in exposure from region to region. Topramezone is a carotenoid biosynthesis inhibitor, non-target plants actively biosynthesizing carotenoids (green photosynthesizing tissues) at the time of application could be potentially at risk if exposed to topramezone.

For an ecological risk assessment at the screening level, the ecosystems that are modeled are intended to be generally representative of any aquatic or terrestrial ecosystem in or adjacent to where topramezone might be used. In the aquatic risk assessment, exposure concentrations were estimated with the Tier II simulation models PRZM and EXAMS, whereas the terrestrial risk assessment used the Tier I model estimates, T-REX for birds and mammals and TerrPlant for terrestrial plants. The specific receptors addressed in the ecological risk assessment are shown in the Conceptual Model (Figure II.2). In general, fish and aquatic invertebrates in both freshwater and estuarine/marine environments are represented in aquatic assessments. Three different size classes of small mammals are represented, along with four potential foraging categories are represented in terrestrial assessments.

[12] When a NOAEC value is determined to be statistically greater than the EC25 value, the EC05 is used instead.

III Analysis

A. Use Characterization

The proposed name for the end-use product containing topramezone as the single active ingredient is "BAS 670 H 336 SC Post-emergent Corn Herbicide"[13] It is a soluble concentrate that contains 29.7% topramezone as the only active ingredient. The product is to be used as a selective, systemic herbicide to control emergent weeds (grasses and broadleaf weeds) on corn.

This end-use product is being proposed for uses on field corn (i.e., corn grown primarily for animal feed or market grain), popcorn, seed corn, and sweet corn. "BAS 670 H 336 SC Post-emergent Corn Herbicide"can be used on conventional and herbicide resistant/tolerant hybrids,, such as Clearfield®, Roundup Ready®, and LibertyLink® corn. The proposed methods of application are ground and aerial.

Table III-1 summarizes key information contained in the proposed label dated December 2004. This Table served as the basis for selecting the appropriate application rates and methods used as part of the input parameters needed to obtain EECs with simulation models and to identify label deficiencies.

Table III.1 Label Information for the Proposed End-use Product "BAS 670 H 336 SC Post-emergent Corn Herbicide", Dated December 2004.

Type of Information	Label Information	Comment
Time of Application	Apply when weeds are actively growing. Weed height specified in the label for optimal control Apply a minimum of 1 hour before rainfall or overhead irrigation Can be applied up to 45 days prior to corn harvest Conservation tillage as well as conventional tillage production systems Do not apply through irrigation systems	The following information is also contained in the proposed label: BASF has not tested all sweet corn or popcorn hybrids or seed corn inbred lines for tolerance (recommends contacting local seed supplier for tolerance information. Avoid disturbing treated areas for at least 7 days after application The product should be applied during favorable growing conditions, for crops under environmental stress are most likely to experience injury. The sign of injury is transient (temporary) bleaching at leaves intercepting the spray application

[13] At the time of this assessment, no Trade Name has been assigned for the end-use product.

Type of Information	Label Information	Comment
Method of Application	Ground (ground equipment; flat nozzles). Avoid spraying when wind speeds are > 15 mph or during periods of temperature inversions Aerial	Aerial: Provides some , but not sufficient, guidance
Application Rate Frequency of Application	0.011 - **0.022** lbs ai/acre (12.35 - **25** g/ha) Split applications (2) are allowed, but not to exceed 25 g/ha per growing season and allowing 7 days between sequential application	No comment

Additives: a. Fertilizer b. Adjuvant	An adjuvant AND a nitrogen fertilizer source are required to achieve optimum weed control a. Fertilizer The label recommends that the nitrogen based fertilizer include urea ammonium nitrate (UAN; 28 to 34% and 10-34-0 at a minimum rate of 1.25 gallons/100 gallons of water (i.e., 1.25% v:v). Spray grade ammonium sulfate (AMS) may be used at a minimum rate of 8.5 lbs/100 gallons of water. Do not use a liquid fertilizer b. Adjuvant Petroleum -based or vegetable- seed based oil concentrate or methylated seed oil. Crop oil concentrates or methylated seed oils are to be used at a rate of 1.25 gallons/100 gallons water (i.e., 1.25%) "Agriculturally approved" drift reducing additives may be used Water is the only carrier that is recommended	**No comments**

Other Herbicides Recommended as Potential Tank Mixes Other Herbicides Recommended as Potential for Sequential Applications	Atrazine (0.25 to 1.0 lb (per acre) Is recommended for better weed control 2,4-D; Accent, Atrazine, Clarity, Bicep II Magnum; Bicep Lite II Magnum, Buctril; Distinct, Dual II Manum, -Max Lite; Guardsman Max; Harness; Harness Xtra; Hornet; Keystone; Keystone LA; Liberty; Lightning; Marksman; Option; Outlook; Prowl; Roundup UltraMax; Steadfast; Stiner; Surpass; TopNotch; Tough Use of BAS 670 336SC as a sequential post-emergence treatment following a pr-eemergence grass herbicide, such as Outlook, Prowl, Guardsman, Max, Dual II Magnum, Harness, or Surpass BAS 670 336SC may also be used in sequential programs with registered burn-down herbicides	**BAS 670 336SC should not be mixed with an herbicide with the same mode of action as topramezone (see "Mode of Action")** **The label says that use of a crop oil or methylated seed oils in tank mixtures of BAS 670 336SC plus 2,4-D, Clarity, Distinct, or Marksman may result in crop injury if applied during periods od cold, wet weather or hot and/or humid weather. In such cases, a nonionic surfactant is recommended**
Mixing Order	Fill spray tank (½ to 3/4 full with water Add other soluble packet products- mix thoroughly Add BAS 670 336SC Add WP, DG, DF, or LF formulations Add emulsifiable concentrate (EC) products (not specified which EC) Add adjuvant Add liquid fertilizer Agitate and fill the tank with water	No comment
Buffer Zone	Not specified in the label	
Replanting post-application	All field corn types, field corn grown for seed, sweet corn, popcorn...................... ANYTIME Cereal crops (wheat, barley, oats and rye, winter canola........ THREE MONTHS Alfalfa, cotton, canola, peanuts, sorghum, soybeans, sunflower, edible beans and peas, potato...... NINE MONTHS All crops not listed above........ EIGHTEEN MONTHS	

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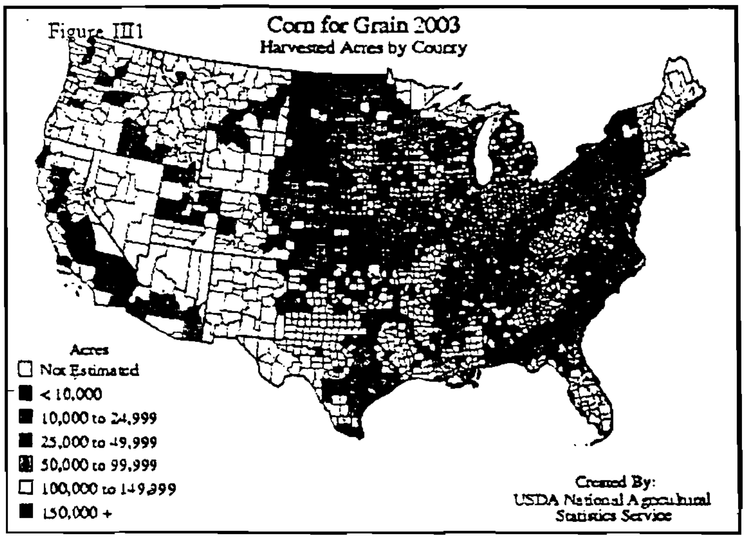
Environmental Hazard Statement in the proposed label	Do not apply directly to water or areas where surface water is present, or to inter-tidal areas below the mean water mark. Do not contaminate water when disposing of equipment wash water **Do not apply through any type of irrigation system** Product must be used in a manner which will prevent back siphoning in wells, spills or improper disposal of excess pesticide, spray mixtures or rinsate	
Other Warnings/Restrictions/	In addition to maximum application per season, no application within 45 days harvest, the following warnings/restrictions also appear in the proposed label: Label restrictions for other herbicides used in tank mixtures must be followed No grazing or feeding (treated corn forage, silage, fodder, rain) for at least 45 days after application	

Other Recommendations	Other Herbicides	Comments
Other Herbicides Recommended as Tank Mixes	Atrazine (0.25 to 1.0 lb per acre is recommended for better weed control 2,4-D; Accent, Atrazine, Clarity, Bicep II Magnum; Bicep Lite II Magnum, Buctril; Distinct, Dual II Manum, -Max Lite; Guardsman Max; Harness; Harness Xtra; Hornet; Keystone; Keystone LA; Liberty; Lightning; Marksman; Option; Outlook; Prowl; Roundup UltraMax; Steadfast; Stiner; Surpass; TopNotch; Tough	**BAS 670 336SC should not be mixed with an herbicide with the same mode of action as topramezone (see "Mode of Action"), such as isoxaflutole or mesotrione. They should only be used in rotation with topramezone.** The label says that use of a crop oil or methylated seed oils in tank mixtures of BAS 670 336SC plus 2,4-D, Clarity, Distinct, or Marksman may result in crop injury if applied during periods od cold, wet weather or hot and/or humid weather. In such cases, a nonionic surfactant is recommended
Potential Herbicides for Sequential Applications	Use of BAS 670 336SC as a sequential post-emergence treatment following a pre-emergence grass herbicide, such as Outlook, Prowl, Guardsman, Max, Dual II Magnum, Harness, or Surpass BAS 670 336SC may also be used in sequential programs with registered burn-down herbicides	BAS 670 336SC should not be mixed with an herbicide with the same mode of action as topramezone



Potential Use Areas

Corn is a major crop in the United States (Figure III 1). In 2004, corn planted area for all purposes was estimated at 81.0 million acres, up 3 percent from both 2002 and 2003. The percent of corn planted for grain/seed, "sweet corn" (market fresh; processing), and popcorn varied by state. Field corn is predominantly grown in the Midwestern United States. While sweet corn is also grown within the Corn Belt, the Eastern United States are major the growers of sweet corn.

Besides the difference in soils and climates, there is also a major difference between field and sweet corn, as harvesting time depends on the degree of moisture of the grain. Therefore, the time intervals between planting, post-planting weed emergence, and harvest can exhibit a wide range of spatial and temporal variability in post-emergence applications.

http://www.usda.gov/nass/graphics/county03/crhar.htm

Planting and Harvesting

http://www.usda.gov/nass/pubs/uph97.htm)

The extensive spatial and temporal variability in corn cultivation can be inferred from the summaries presented below for popcorn, sweet corn, and "grain" corn. Thus, time of weed emergence (when a post-emergence herbicide, such as topramezone, will be used), is expected to be dependent on the time of planting.

a. Popcorn:

Popcorn cultivation is predominantly centered in the upper Midwestern States, of which Indiana and Nebraska are major producing states. Other states include Illinois, Iowa, Kansas, Kentucky, Michigan, Missouri, and Ohio. Popcorn is also grown in Alabama, Oklahoma, New Jersey, Maryland, Oregon, Pennsylvania, South Dakota, Tennessee, Virginia, and Wisconsin.

Popcorn grows best in deep fertile soils, moderate rainfall, and temperate weather. Fields are planted from April 15 (southern regions) to May 25 (northern regions). Most of the popcorn is irrigated. Popcorn (*Zea mays everta*) has a very hard endosperm. The criteria for harvesting popcorn is crop maturity and optimal moisture content Harvest may occur during an extended period, typically from mid-September to early-December, depending on the region..

http://www.ipmcenters.org/cropprofiles/docs/us-ncr-popcorn.html

b. Sweet Corn:

Sweet corn is planted as a fresh market vegetable or for processing. Unlike popcorn or grain corn, sweet corn must be harvested within a very short time for optimal maturity and moisture.(average 70 to 85 days after planting, that is in less than 3 months). Thus, planting dates are staggered over periods of weeks to extend the harvesting period.

The Eastern states are the major growers of fresh-market sweet corn, with California as the major producer in the West. In the North Central region, most of the sweet corn grown for processing falls within twelve states, mainly from western Indiana through northern Illinois and southern Wisconsin and Minnesota. The optimal cultivation conditions are deep fertile soils, moderate rainfall, and temperate weather. Early planting dates is 1 to 2 weeks before the frost-free date for a particular area, but may extend to early July.

http://www.ipmcenters.org/cropprofiles/docs/us-ncr-sweetcorn.html

Florida is a major producer of fresh-market sweet corn. Most of the Florida sweet corn is grown in farms that also produce other vegetables, row crops, pasture, and forage crops. Palm Beach county is the major producing region, but Miami-Dade, Collier, and Hendry Counties are also significant growing areas. In Florida, sweet corn seeds may be planted at any time from August through April, depending on the production region. In South Florida, it is typically planted from October to March. Sweet corn harvest can occur from mid-November through mid-July, with an active harvest period from April to May.

http://www.ipmcenters.org/cropprofiles/docs/FLSweetcorn.html

c. Grain corn

The U.S. Corn Belt[14] comprises Illinois, Indiana, Iowa, Kansas, Kentucky, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin.

Planting in Texas can begin as early as the end of February and extends until the middle of June. In most of the southern states in general, the planting window is from early March to no later than the middle of May. In the Corn Belt states, most of the corn is planted after the middle of April and may extend until no later than the middle of June. In the Northern states, most of the corn is planted from May to June. The end of the harvest period may extend up to the middle of December. The span between planting and harvesting are longer than for sweet corn because grain corn must have a lower moisture content than sweet corn.

B. Exposure Characterization

1. Environmental Fate and Transport Characterization

Summary

Biotransformation (soils; water-sediments) is the major route of dissipation of topramezone in the environment, although it appears that adsorption competes with biotransformation.. Differences in persistence, nature, and relative ratio of transformation products were found in aerobic soils. The metabolite "M670H05"was identified as the major metabolite in some, but not all, of the aerobic soils. Both topramezone and "M670H05" can be persistent in aerobic soils (pseudo-first order, linear half-lives > 125 days in most soils). Under environmental conditions, abiotic hydrolysis and direct photolysis in water are not important transformation pathways for topramezone.

Metabolites formed in aerobic soil were markedly different from those found in water-sediments. Moreover, metabolites were also different in anaerobic and aerobic water-sediments. Major differences in persistence of topramezone were found between two aerobically incubated water-sediments test systems (half-lives < 20 days in a pond water, but > 120 days in river water), but the reasons for these differences are not clear.

[14] The U.S. Corn Belt is the largest, contiguous agro-ecosystem in the world capable of supporting corn production.

Topramezone exhibits high to moderate mobility in soils. Its major soil metabolite "M670H05" is highly mobile in soils. Topramezone does not have the potential to volatilize from soils or water nor to bioaccumulate in fish or other aquatic organisms.

General Note: Soil, sediments, and water characterization appear in Appendix B.2

a. Persistence

Topramezone is stable towards abiotic hydrolysis (pH 5, 7, and 9; 25° C; 45902416). Direct photolysis in water is not an important degradation pathway for toprãmezone (half-life 132 days based on a 12 hrs light/dark cycle, Spring sunlight at 40° latitude North; 45902417). Photolysis on soil is not a significant degradation pathway for topramezone (45902418).

The overall dissipation of topramezone in soil and water-sediment systems is likely to involve two different processes, namely biotransformation and time-dependent sorption and it appears that time-dependent sorption may play a significant role. However, biotransformation is involved in the formation of metabolites. Even though microorganisms control metabolite formation, topramezone has the potential to be persistent in aerobic soils, as can be seen from the half-lives in Table III-2. For all studies involving soils and water-systems, half-life calculations were based on extractable radioactivity.

Aerobic soil metabolism studies with topramezone as the test substance were conducted in six USA soils of various textures and different collection sites representative of potential corn growing areas. Table III-2 summarizes persistence data (as linear half-lives and DT50[15]) of topramezone in the six study soils. The variability in persistence among the soils is likely a reflection of differences of microbial activity. In addition, a separate aerobic soil metabolism study (one soil) was conducted with the major aerobic soil metabolite M670H05 (i.e., a metabolite found at > 10% of the applied radioactivity) as the test substance (45902420). Although this metabolite was not form in large amounts in all soils and it did not exceed 16% of the applied radioactivity after 1 year incubation in any of the soils, the observed half-life was as high as 1 year. When topramezone was used as the test substance, the amount of M670H05 increased with time throughout the 1-year study, but it is not known if it continues to increase after 1 year.

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[15] The aquatic exposure models (GENEEC; PRZM and EXAMS, and SCI-GROW) use pseudo-first order, linear half-lives as input paramaters and not DT50. Half-lives are equal to the DT50 if and only if a reaction follows first order kinetics. In addition, only kinetics data derived from laboratory studies are used in selecting input parameters for simulation modeling. Field data are not used as input parameters

Table II.2 Persistence of Topramezone in Soils Incubated under Aerobic Conditions at 27° C (45902419; 45902421)

Data	Loam from Idaho	Silt loam from Indiana.	Loam from Iowa.	Clay loam from Minnesota.	Silt loam from South Dakota	Sandy loam from North Carolina
Linear half-life (0-383 days)	181.3 days (r2 = 0.886).	182.0 days (r2 = 0.958).	301.5 days (r2 = 0.848	124.5 days (r2 = 0.924).	195.9 days (r2 = 0.942)	Observed: > 364 days
DT50 (empirical data)	100- 160 days	125 days	290 days	90-150 days	110 days	> 364 days

Although there are some deficiencies in the studies conducted with water-sediment systems, the persistence of topramezone in water-sediment systems appears to be shorter than in aerobic soils (half-life of 13 to 24 days in total system, anaerobic conditions; and 19 to 24 days in one aerobically incubated system). Marked differences in persistence were observed between the two aerobically incubated water-sediment systems (Table III.3). Under aerobic conditions, topramezone was more persistent in the river water system (half-life > 120 days) than in the pond water system (half-life of total system, 19 to 24 days). Considerable differences were observed in some of the physical and chemical properties of the river and pond water. For example, the pond water was considerably higher in hardness, electrical conductivity (an indication of a high content of ionic species), and total dissolved solids when compared with the river water. How these differences in between pond and river water systems affect the persistence of topramezone in aerobic water-sediment systems is not known. However, it is reasonable to assume that considerable variability in persistence and nature/ relative amounts of metabolites is expected throughout the widespread potential use areas. The petitioner has been requested to address and clarify the deficiencies identified in all of the water-sediment studies.

Table III.3 Persistence of Topramezone in Water-Sediment Systems Incubated Under Anaerobic (459024-22) and Aerobic (45902423) Conditions

Water-Sediment Conditions	Water-Sediment System	Half-lives (Linear); (R2)
Anaerobic	Lake reservoir in South Dakota; silt loam sediment	Linear/Natural log Water: 11 to 18 days (0.880 to 0.932) Sediment (Not calculated) Total system: 13-24 days (0.849 to 0.917) DT50 (empirical): 7-15 days, total system
Aerobic	Non-agricultural river, Ohio; loamy sand sediment	Water, sediment, and total system, > 120 days DT50 (empirical): > 120 days

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Water-Sediment Conditions	Water-Sediment System	Half-lives (Linear); (R2)
Aerobic	Non-agricultural pond, Ohio Loam sediment	Water: 10.7 to 10.9 days (0.926- 0.976) Sediment: 49- 78 days (0.808- 0.8390 Total system: 19 to 24 days (0.968) DT50 (empirical), total system: 14 to 28 days

Although terrestrial field dissipation data are not currently used in models, the results of these studies are summarized in Table III..4. Additional data has been requested from the petitioner to help clarify procedures and data in the storage stability study (45902428)

Table III.4 Persistence of Topramezone End-use Product Under Field Conditions (45902426 and 45902427)

Site and Formulation	Linear Half-life, Days	DT50, Days
Indiana, Bare ground Plot, SC Sandy loam over loamy sand *Ecoregion 8.1*	67	4.2 to 5
South Dakota, Bare ground Plot, SC Clay loam *Ecoregion 9.2*	182	3 to 13
South Dakota, Bare ground Plot, DF Clay loam *Ecoregion 9.2*	158	13 to 17
California, Bare ground Plot, SC Sandy loam *Ecoregion 11.1*	98	5 to 18
California, Cropped Plot, SC Sandy loam *Ecoregion 11..1*	29	19 to 22
Ontario, Canada/Loam cm) over silt loam-silty clay loam *Ecoregion 8.3*	158	29

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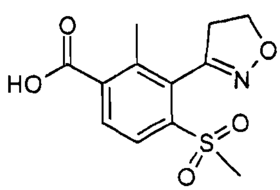
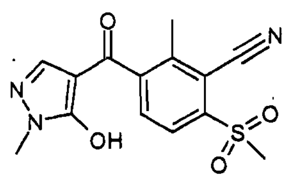
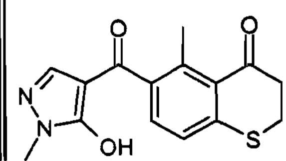
b. Transformation products

The identified metabolites of topramezone are presented in Table III.5. The Table indicates the media and incubation conditions in which they were found, at what percent of the applied radioactivity, how they form, and when they reach a maximum amount Note that metabolite M670H05 is formed only in soils and that the metabolites formed in aerobic water-sediment systems are very different from those encountered under anaerobic conditions. In all the studies involving soils and sediments, "non-extractable" residues increased with time and were predominantly associated with the fulvic acid fraction. A plausible explanation could be that the rate of adsorption to soils/sediment may be faster than the rate of biotransformation. That is, that the rate of adsorption (time-dependent sorption) controls the dissipation of topramezone in soils/sediments.

Table III.5 Metabolites of Topramezone

Metabolite and Company Code	Chemical Name	Formation	Detection (As Percent of the Applied Radioactivity)
 M670H05 (BAS 670 H acid Like topramezone, this metabolite is also a weak acid	3-(4,5-Dihydro-isoxazol-3-yl)-4-methanesulfonyl-2-methyl-benzoic acid CAS Reg. No: 223646-24-0	Cleavage of the -C (pyrazol)-C(keto)- bridge This is the only cleavage metabolite identified for topramezone. This metabolite retains the isoxazol ring	Major soil metabolite, but the amount varied among the 6 soils (aerobic). It was found at a maximum of 16% only in a clay loam soil from Minnesota after 279, but at < 10% in some of the other soils. The amount of this metabolite increased with time and was not detected before 97 days in any of the soils It was not found in any of the water-sediment systems (anaerobic; aerobic). The transformation products identified in water-sediment systems cannot form M670H05 nor can this metabolite form the water-sediment metabolites

Metabolite and Company Code	Chemical Name	Formation	Detection (As Percent of the Applied Radioactivity)
 M670H01 (BAS 670 H cyano) Note: The cyano group can potentially hydrolyze to an amide and/or to carboxylic acid group. Neither the amide nor a carboxylic acid form for "M670H01" were detected	[3-Cyano-4-methane-sulfonyl-2-methyl-phenyl](5-hydroxy-1-methyl-1H-pyrazol-4-yl)methanone.	Isoxazol ring opening	Found only in one of the aerobically incubated soils (Idaho loam), at 10.3% Found at a maximum of 10.2% in pond water-loam sediment (OH) under aerobic conditions. This metabolite was predominantly associated with the sediment
 M670H10	6-[(5-Hydroxy-1-methyl-1H-pyrazol-4-yl)carbonyl]-5-methyl-2,3-dihydro-4H-1-benzothiopyran-4-one.	Elimination of the isoxazol ring and formation of a 4-one- thiopyran (heterocyclic) ring Reduction of S(VI) of the sulfonyl group to S(-II) in the thiopyran ring. This is consistent with what would be expected in anoxic water-sediment systems	This metabolite was only found water-sediment under anaerobic conditions, at 16% in water, 26 -34% in sediment.
$^{14}CO_2$	Carbon dioxide	Mineralization	Maximum of 14% only in the Idaho loam soil (aerobic) after 388 day

Although no physical and chemical properties were submitted for the metabolites, these were estimated using the structure-activity relationship EPIWIN 3.1 program (Estimation Programs Interface) Suite™, Version 3.10)[16] Appendix B.3 summarizes the EPI estimates for these metabolites and a description of the program.

The EPIWIN-estimated physical and chemical properties for topramezone are in agreement with the experimental data. The Log Kow of MH670H05 is 2.75 (just below the trigger for bioaccumulation potential), that is, it is the most hydrophobic of the metabolites and the one

[16]The EPI (Estimation Programs Interface) Suite™ is a Windows® based suite of physical/chemical property and environmental fate estimation models developed by the EPA''s Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC). EPI Suite™ uses a single input to run the following estimation models: KOWWIN™, AOPWIN™, HENRYWIN™, MPBPWIN™, BIOWIN™, PCKOCWIN™, WSKOWWIN™, BCFWIN™, HYDROWIN™, and STPWIN™, WVOLWIN™, and LEV3EPI™. EPI Suite™ was previously called EPIWIN

having the highest binding coefficients, which is consistent with the results of the batch-equilibrium adsorption/desorption studies.

As discussed under the "Mode of Action" section, the two major molecular structure features of 4-HPPD inhibitors (e.g., topramezone, isoxaflutole, and mesotrione) are centered on the carbonyl (keto) groups. At least one of the carbonyl groups must be attached to a substituted benzoyl group and at least one of the carbonyl groups can form a stable enolate (i.e., a stable enol tautomer; keto-enol tautomerism). This class of compounds ("ketonates") chelate with Fe(II), the active site of the 4-HPPD dioxygenase enzyme. Chelation via ketonato ligands to Fe(II) is well known[17]

The metabolites "M670M01" (cyano metabolite) and "M670H10" preserve the carbonyl group and the enolate in the pyrazole ring. Based on these structural features, these two metabolites are potential 4-HPPD inhibitors. Furthermore, "M670H10" also has an additional carbonyl group at C-4 of the thiopyran ring, which can potentially form the enolate.

The metabolite "M670H01" (the cyano (nitrile) metabolite) also have the potential to bind to Fe(II) via the cyano (nitrile) group. "M670H01" is structurally very similar to an active degradation product of isoxaflutole (RPA-202248; also a "ketonitrile").

c. Transport

Batch-equilibrium adsorption/desorption studies were conducted with topramezone, the major soil metabolite "M670H05", and the anaerobic aquatic metabolite "M670H10" as the test substances. The same six soils used in the aerobic soil metabolism study were used for the adsorption/desorption studies. The results for the adsorption phase (Freundlich adsorption coefficients, organic -carbon normalized coefficients, and 1/N) are summarized in Table III.6.

Of The most mobile of these chemical species are topramezone and M670H05, both of which can be carried to surface water by runoff and/or ground water by leaching. The two weak acids, topramezone and "M670H05", did not bind strongly to most soils, but both adsorbed stronger in the Minnesota clay loam and North Carolina sandy loam than in any of the other soils. The weakest adsorption for parent and the two metabolites was observed with the Idaho loam soil. The anaerobic water-sediment metabolite "M670H10" adsorbed stronger than the weak acids and was predominantly associated with the sediment phase (anaerobic conditions). This is a metabolite formed *in-situ* (i.e., in the water-sediment system) and therefore, will not be carried to surface water by runoff or leach in the field. Based on EPIWIN estimates, M670H01 (the cyano metabolite) could be as mobile as parent or M670H05.

[17] Cotton, F.A. and Wilkinson, G. Advanced Inorganic Chemistry, Fifth Edition, 1988, Wiley Interscience, New York

Table III.6 Adsorption Behavior of Topramezone, the Aerobic Soil Metabolite M670H05 (45902425) and the Anaerobic Aquatic Metabolite M670H10 (46242703) on Six Soils No appreciable adsorption (n/a)

Sorption Coefficients	Idaho	Indiana	Iowa	Minnesota	South Dakota	North Carolina
Soil Texture	Loam	Silt loam	Loam	Clay loam	Silt loam	Sandy loam
Kads, Freundlich: a. Parent b. M670H05 c. M670H10	a. 1.40 b. n/a 1 c. 10.6	a. 2.30 b. n/a c. 4.3	a. 1.97 b. n/a c. 19.5	a. 4.87 b. 9.4 c. 52	a. 2.59 b. n/a c. 23.9	a. 3.69 b. 5.71 c. 61
Koc a. Parent b. M670H05 c. M670H10	a. 38 b. n/a c. 377	a. 284 b. n/a c. 857	a. 53 b. n/a c. 807	a. 120 b. 134 c. 1,292	a. 91 b. n/a c. 1,219	a. 303 b. 235 c. 5,675
1/N a. Parent b. M670H05 c. M670H10	a. 0.875 b. n/a c. 0.9	a. 0.823 b. n/a 0.8	a. 0.863 b. n/a c. 0.9	a. 0.859 b. n/a c. 0.9	a. 0.850 b. 0.920 c. 0.9	a. 0.802 b. 0.885 0.9

In theory, the mobility of the two weak acids (topramezone and "M670H05") should increase with increasing pH. However, the pH of all of the soils ranged from 5.7 to 6.8. Therefore, the pH-dependence of adsorption could not be established from such a narrow range. Adsorption did not appear to correlate with cation exchange capacity or type of clay, although it appears to be some correlation with the percent of organic matter content. Although topramezone is likely to be highly dissociated within that pH range, the sorptive behavior of the undissociated form is not well established. An invalid test on the toxicity of topramezone to a non-vascular plant was higher at pH range of 4.1- 5 than that observed for other species at neutral pH. It is unclear if the increased toxicity is related to undissociated topramezone or simply to a pH effect. The test is considered invalid because the pH was out of the acceptable range.

In all of the metabolism studies, the amount of "non-extractable" radioactivity associated with soil or sediment increased with time. The "non-extractable"radioactivity was found to be predominantly associated with the fulvic acid fraction. Thus, it is possible that the overall dissipation of topramezone in soils and water-sediments may depend on competitive biotransformation and time-dependent adsorption processes. The batch-equilibrium adsorption/ desorption studies are short duration studies and are not currently designed to determine the kinetics of sorption (i.e., how fast a chemical adsorbs to or desorbs from soils). Therefore, the contribution of time-dependent adsorption to the overall dissipation of topramezone cannot be established. In sediments, the majority of "lost radioactivity" appears in the non-extractable sediments, suggesting that it may bind quickly with sediments, where it may remain relatively unchanged for at least one year. A qualitative discussion on binding of topramezone to soil and sediment is contained in the "Risk Description" section.

Topramezone has a low potential to volatilize from soils or water, as suggested by its low vapor pressure and the calculated Henry's Law Constant.

d. Accumulation

Based on the pH-dependent *n*-octanol/water partition coefficients (< − 0.8), topramezone has a low potential to bioaccumulate in fish within the environmentally significant range of 5 to 9. In a fish bioaccumulation in fish study (45902322) conducted at a exposure level of 0.030 mgL-1, the Bioconcentration Factors (BCF) were 0.30, 0.69, and <0.048 for the whole fish, non-edible tissues, and edible tissues, respectively. Of all the metabolites that may form in water-sediments, "M670H10" (anaerobic conditions) is the most hydrophobic. Parent topramezone, "M670H05", and "M670H01" have very low *n*-octanol/water partition coefficients (Log Kow < 1). The EPIWIN-estimated Log Kow for "M670H10" is 2.75.

In aerobic soil metabolism studies (1-year duration), the amount of the metabolite M670H05 increased with time, but it is not known if it keeps increasing beyond 1 year after application. Considering that M670H05 is a persistent metabolite (half-life 56 days to > 1 year), its potential to accumulate in the field cannot be ruled out. In addition, if one considers soils as a reservoir for topramezone based on the observed time-dependent increase in non-extractable residues there is a potential for carryover of topramezone from season to season as noted by long rorational crop intervals recommended in the label. Although it may be argued that these residues are not bioavailable, they may become bioavailable if they desorb slowly as parent topramezone and/or potentially active metabolites. Long-term behavior of non-extractable residues of pesticides is not well understood, but recent data for two sulfonylurea herbicides (chlorsulfuron and metsulfuron) suggest that these two herbicides remain "intact" in the fulvic acid fraction of the soil. The long-term phytotoxicty of soils associated with some sulfonylurea herbicides has been attributed to the slow release (desorption) of the intact herbicide associated with the fulvic acid fraction[18]. A similar behavior cannot be ruled out for topramezone.

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18 Gao. J. and Sun, J. 2002..*Studies on bound ^{14}C-chlorsulfuron residues in soil.* **J. Agri. Food Chem.** 50(8), pp 2278-82.

Ye, Q., Sun, J., and Wu, J. 2003. *Causes of phytotoxicity of metsulfuron-methyl bound residues in soil.* **Environ. Pollut.**, 126(3), 417-23.

2. Measures of Aquatic Exposure

Figure III3 summarizes the chemical species that may be found in anaerobic and aerobic water-sediment systems. The figure indicates the routes by which each could enter to or form in aquatic media. Note that the soil metabolite M670H005 can only enter an aquatic system by runoff/soil erosion. This metabolite was not found in water-sediment studies.

Anaerobic Water-Sediment Systems

Parent (Run-off; Spray Drift)

Metabolite **M670H10** (formed in the water-sediment system)

Soil Metabolite M670H05 (Run-off)

Aerobic Water-Sediment Systems

Parent (Run-off; Spray Drift)

Metabolite **M670H01 (BAS 670 H cyano)-** (Formed in the water-sediment system; Run-off from soils)

Soil Metabolite M670H05 (Run-off)

Figure III.3

This figure represent the potential chemical species to which aquatic organisms may be exposed and by which route they may enter surface water. Note that the cleavage metabolite "M670H05" appears to form only in aerobic soils and can enter surface water only by run-off and/or wind-blown soil. Metabolite "M670H10" was found only in anaerobic water-sediment systems (i.e., *in situ* formation), while "M670H01" could form in soil and enter the water body by runoff and/or form *in situ* in aerobic water-sediment systems. Therefore, the only chemical species that may enter surface water by spray drift is topramezone. Once all these chemical species are present in surface water, they may further transform and/or partition into the water column or the sediment according to their binding behavior. However, the data from the submitted studies indicate that non-extractable residues in soil and water-sediments increase with time, with the concomitant decrease of parent topramezone. Thus, "disappearance" (i.e., overall dissipation) of topramezone may be a result of time-dependent adsorption competing with biotransformation. The metabolites "M670H01" and "M670H10" have the potential to be 4-HPPD inhibitors.

1. Aquatic Exposure Modeling

Since toxicity to plants was anticipated for topramezone, exposure concentrations of topramezone surface water were estimated using Tier II simulation models, PRZM Version 3.12 (beta compiled(05/24/01, Carsel, 1997) and EXAMS (Vers. 2.98.04 compiled 07/18/04, Burns, 2002) [19] for surface water. PRZM simulates pesticide fate and transport as a result of leaching, direct spray drift, runoff and erosion from an agricultural field and EXAMS estimates environmental fate and transport of pesticides in to a surface water body for a 30-year period (1961 to 1990). PRZM and EXAMS were linked by the program (PE4-PL, vers. 01)

The EECs for surface water generated by PRZM-EXAMS typically represent a range of exposure scenarios from pesticide use on a particular crop or noncrop use site. Estimates were made for aerial and ground applications and at the maximum proposed applications rates and for single and split applications. Ten different, standard corn cropping scenarios were selected for these estimates.

Application rates were taken from the proposed label. Appropriate input parameters were selected from the physical and chemical properties (intrinsic properties) and from environmental fate studies[20] submitted in support of registration for this chemical. Selection of physical chemical properties and environmental fate input parameters were in accordance with the recommendations given in *Guidance for Selecting Input Parameters in Modeling the Environmental Fate and Transport of Pesticides*, Version II, February 28, 2002. Estimates were made for aerial and ground applications and at the proposed applications rates.

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19 See http://www.epa.gov/oppefed1/models/water/index.htm for detail description of the simulation models and guidelines for selecting input parameters

20 Unlike the intrinsic, physical and chemical properties, environmental fate parameters are extrinsic properties that are specific to the test media and conditions of the studies (e.g., type of soil, temperature, moisture)

Scenarios

The standard scenario for ecological exposure simulates the fate of a pesticide transported as a result of runoff and erosion, and or spray drift from an 10-ha agricultural field directly into a surface water body (PRZM). The small field is assumed to be 100% cropped. The surface water body in which the EECs are simulated (EXAMS) is the standard pond (10,000-m2 pond, 2-m deep). Topramezone is a new chemical and therefore, there are no specific aquatic monitoring data that can be used in the aquatic exposure. The ten scenarios (Table III.7) were chosen as representative corn-growing sites where topramezone may be used (Leovey, 2002)[21] The "Florida sweet corn scenario" was of particular interest because Florida sweet corn is grown primarily in counties around the Everglades (e.g., Palm Beach County).

Table III.7 Ten standard corn scenarios used in the aquatic exposure assessment.

Corn Scenario	Location	Met File
California Corn	Stanislaus/San Joaquin Counties in the Central Valley	w23232.dvf
Florida Sweet Corn	Palm Beach County	w12844.dvf
Illinois Corn	McLean County	w14923.dvf
Mississippi Corn	Southern Mississippi Valley Uplands	w13893.dvf
North Carolina Corn East	Pitt County	w13722.dvf
North Carolina Corn West	Henderson County.	w03812.dvf
North Dakota Corn	Pembina County in the Red River Valley	w14914.dvf
Ohio Corn	Darke and/or Pickaway Counties	w93815.dvf
Pennsylvania Corn	Lancaster County	14737.dvf
Texas Corn	Claypan area, Milam County	w13958.dvf

Input Parameters

Environmental fate data and physical and chemical properties (Table III.8) were selected from the submitted studies in accordance with *Guidance for Selecting Input Parameters in Modeling the Environmental Fate and Transport of Pesticides*, Version II, February 28, 2002. Detailed description, documentation, and direct links for running these models can be found in:

http://www.epa.gov/oppefed1/models/water/index.htm

[21] Leovey, Elizabeth. 2002. PRZM Standard Crop/Location Scenarios, Procedure to Develop and Approve New Scenarios, and PRZM Turf Modeling Scenarios to Date. February 27, 2002. USEPA. OPP. Environmental Fate and Effects Division, Arlington, VA

Table III.8 Input Parameters Selected to Run the PRZM and EXAMS Models[22].

Parameter	Value/Selection criteria	Source
Maximum Application Rate per Season, lb ai/acre (g/ha)	0.022 lb topramezone/acre (25 g topramezone/ha) Can also be applied in 2 sequential 0.011 lb ai/acre per applications, 7 days apart, but not to exceed 0.022 lbs ai/acre per season	Proposed label of end-use product BAS 670 336SC
Application Method and Depth of Incorporation (cm)	Ground Aerial No incorporation (model default 4-cm)	Proposed label of end-use product BAS 670 336SC
Soil Partition Coefficient (Kads; mL/g)	mean Kads = 2.8 (n = 6; 1.40, 2.30, 1.97, 4.87, 2.59, 3.69)	45902425
Aerobic Soil Metabolism Half-life (days) [Linear T½]	241.28days (90th percent upper bound of mean) (n=5; 181.3, 182.0, 301.5, 124.5, 195.9)	45902419; 45902421
Spray Drift Fraction (ground spray / aerial)	ECO: 0.01/ 0.05	Model
Application Efficiency (ground spray / aerial)	0.99 / 0.95	Model
Molecular Weight, Daltons	363.39	Physical and Chemical Property
Vapor Pressure	7.5 * 10-13 torrs	Physical and Chemical Property
Henry's Law Constant	2.39 * 10-17 atm-m-3mol^{-1} @ 20 °C	Estimated
Solubility in Water at 20oC Topramezone is a weak acid (pKa 4.6) The solubility of topramezone is pH dependent	15,000 mgL^{-1}	Physical and Chemical Property

22 Based upon the aerobic aquatic degradation from the Grand River. Aerobic aquatic metabolism was available for two water bodies (Grand River and Homestead Pond - both in Ohio). The half-life was > 120 days in a 120 day study (both rings and all systems: water, sediment, total) in Grand River Water and less than for 25 days (19.0 and 24.2 days for the two different labeled rings) for the total systems (sediment half-life was 49.2 to 77.7 days) in the Homestead Pond. The reason(s) for apparent differences in aerobic aquatic metabolism between water sources could not be determined. But the chemistry of the Homestead Pond water (high salinity - 10.65 mmhos/cm, high dissolved solids - 6,044 mg/L) and sediment acidity (pH < 5) does not appear to be representative of naturally occurring water body. More information concerning the water/sediment source is needed before this information would be considered in the assessment.

Parameter	Value/Selection criteria	Source
Aerobic Aquatic Metabolism Half-life (days)	01 - stable The default value was used because uncertainty in the results for aerobic water-sediment systems 482.56 days [3]	45902422 Data uncertain
Anaerobic Aquatic Metabolism Half-life (days)	30.52 days 90th percent upper bound of mean total system (13.4 and 18.6 days)	45902423
Hydrolysis Half-life @ pH 7 (days)	Stable	45902416
Aquatic, Direct Photolysis Half-life @ pH 7	Stable	45902417

[1] Henry's Law Constant is calculated by EXAMS if Vapor Pressure is entered. Henry's Law Constant is only given to aid in an appreciation of the limited potential for losses through volatilization.

[2] Based upon the aerobic aquatic degradation from the Grand River. Aerobic aquatic metabolism was available for two water bodies (Grand River and Homestead Pond - both in Ohio). The half-life was > 120 days in a 120 day study (both rings and all systems: water, sediment, total) in Grand River Water and less than for 25 days (19.0 and 24.2 days for the two different labeled rings) for the total systems (sediment half-life was 49.2 to 77.7 days) in the Homestead Pond. The reason(s) for apparent differences in aerobic aquatic metabolism between water sources could not be determined. But the chemistry of the Homestead Pond water (high salinity - 10.65 mmhos/cm, high dissolved solids - 6,044 mg/L) and sediment acidity (pH < 5) does not appear to be representative of naturally occurring water body. This issue is discussed in the Risk Characterization chapter. More information concerning the water/sediment source is needed before this information would be considered in the assessment

[3] Aerobic soil metabolism times two.

Because of the uncertainty of the metabolism of topramezone in the aquatic environment resulting from the two water sources (river and pond) used in the aerobic aquatic metabolism studies and the apparent persistent nature of topramezone in the soils (181 to 301 day half-lives), two approaches were used to obtain an estimate of the metabolism in an aerobic aquatic environment. The first assumed that topramezone was stable (half-life = 0) in an aerobic aquatic environment and second, followed EFED's Model Input Parameter Guidance and assumed that aerobic aquatic metabolism rate was twice as slow as aerobic soil metabolism. Thus, the aerobic aquatic metabolism half-life is obtained by multiplying the aerobic soil metabolism half-life [241.28 days = 90 percent upper bound of mean] times a factor two [the aerobic aquatic metabolism half-life is estimated to be 482.56 days]. An additional aerobic aquatic metabolism study and additional information concerning the Homestead Pond water **would help reduce the uncertainty in the aerobic aquatic metabolism of topramezone**. Additional information concerning the metabolism of topramezone in an aerobic aquatic may result in lower EECs.

Estimated Environmental Concentrations (EECs) for the ten corn scenarios

Table III.9 through Table III.12 provide Tier II surface water EECs. The topramezone concentrations represent, the 1-in-10-year annual exceedence probability for peak, 96-hr, 21-day, 60-day, and 90-day for each scenarios. For each scenario two rows are given; the first assumes no aerobic aquatic metabolism. The second represents concentrations estimated assuming a 482.56 day aerobic aquatic metabolism half-life.

Aerial Applications

Table III.9 EECs for Aerial Applications (Single)

1 - Aerial application at 0.022 lb ai/acre per season. Concentrations are in μgL^{-1}(ppb)					
Scenario	*Peak*	*96-hr*	*21-day*	*60-day*	*90-day*
Florida (Sweet)	1.79	1.79	1.77	1.72	1.62
Florida (Sweet)1	1.15	1.14	1.12	1.09	0.89
California	0.54	0.54	0.53	0.52	0.51
California1	0.35	0.35	0.35	0.34	0.33
Illinois	1.16	1.16	1.15	1.15	1.14
Illinois	0.75	0.75	0.74	0.72	0.7
Mississippi	1.49	1.49	1.48	1.45	1.44
Mississippi1	0.86	0.86	0.85	0.81	0.8
N.Carolina E.	0.78	0.77	0.77	0.76	0.75
N. Carolina E.1	0.45	0.45	0.44	0.43	0.42
N. Carolina W.	1.13	1.13	1.12	1.11	1.1
North Carolina W.1	0.72	0.72	0.71	0.69	0.67
North Dakota	1.02	1.01	1.01	1	0.99
North Dakota1	0.6	0.6	0.59	0.57	0.56
Ohio	0.88	0.88	0.88	0.87	0.86
Ohio1	0.6	0.6	0.59	0.57	0.56
Pennsylvania	0.81	0.81	0.8	0.79	0.79
Pennsylvania1	0.46	0.45	0.45	0.44	0.43

Texas	1.34	1.34	1.33	1.31	**1.3**
Texas1	0.74	0.73	0.72	0.7	**0.68**

[1] Aerobic aquatic metabolism assumed to be equal to 482.56 days (2 x the aerobic soil metabolism half-life).

Table III.10 EECs for Aerial Applications (Split)

2 - Aerial applications at 0.011 lb ai/acre per application, 7 days apart. Concentrations are in μgL^{-1}(ppb)					
Scenario	*Peak*	*96-hr*	*21-day*	*60-day*	*90-day*
Florida (Sweet)	1.94	1.93	1.92	1.9	1.72
Florida (Sweet)1	1.22	1.22	1.2	1.16	0.99
California	0.55	0.55	0.54	0.53	0.52
California1	0.36	0.36	0.35	0.34	0.34
Illinois	1.32	1.31	1.31	1.3	1.29
Illinois1	0.87	0.86	0.85	0.82	0.8
Mississippi	1.46	1.46	1.45	1.43	1.41
Mississippi1	0.85	0.85	0.83	0.8	0.78
N. Carolina E.	0.82	0.82	0.81	0.8	0.79
N. Carolina E.1	0.47	0.46	0.46	0.45	0.44
N. Carolina W.	1.11	1.11	1.1	1.09	1.08
N. Carolina W.1	0.69	0.69	0.68	0.66	0.64
North Dakota	0.98	0.97	0.97	0.96	0.96
North Dakota1	0.59	0.59	0.58	0.56	0.54
Ohio	0.99	0.99	0.98	0.97	0.96
Ohio1	0.66	0.66	0.65	0.64	0.62
Pennsylvania	0.8	0.79	0.79	0.78	0.77
Pennsylvania1	0.45	0.45	0.44	0.43	0.42
Texas	1.37	1.37	1.36	1.35	1.33
Texas1	0.75	0.74	0.73	0.71	0.69

[1] Aerobic aquatic metabolism assumed to be equal to 482.56 days (2 x the aerobic soil metabolism half-life).

Ground Applications

Table III.11 EECs for Ground Applications (Single)

1-Ground Application at 0.022 lb ai/acre per. Concentrations are in μgL^{-1}(ppb)					
Scenario	*Peak*	*96-hr*	*21-day*	*60-day*	*90-day*
Florida (Sweet)	1.69	1.68	1.67	1.61	1.52
Florida (Sweet)1	1.1	1.1	1.09	1.04	0.85
California	0.38	0.38	0.38	0.37	0.37
California1	0.27	0.27	0.27	0.26	0.26
Illinois	0.99	0.98	0.98	0.97	0.96
Illinois1	0.65	0.65	0.64	0.62	0.6
Mississippi	1.34	1.34	1.33	1.31	1.28
Mississippi1	0.8	0.8	0.58	0.57	0.57
N. Carolina E.	0.58	0.58	0.58	0.57	0.57
N. Carolina E.1	0.35	0.35	0.34	0.34	0.33
N. Carolina W.	0.95	0.95	0.94	0.93	0.92
N. Carolina W.1	0.63	0.62	0.62	0.6	0.59
North Dakota	0.79	0.79	0.78	0.77	0.77
North Dakota1	0.47	0.47	0.46	0.45	0.44
Ohio	0.7	0.7	0.7	0.69	0.68
Ohio1	0.49	0.49	0.49	0.47	0.46
Pennsylvania	0.83	0.83	0.82	0.81	0.81
Pennsylvania1	0.47	0.47	0.46	0.45	0.44
Texas	1.2	1.2	1.19	1.18	1.17
Texas1	0.67	0.67	0.66	0.64	0.61

[1] Aerobic aquatic metabolism assumed to be equal to 482.56 days (2 x the aerobic soil metabolism half-life).

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Table III.12 EECs for Ground Applications (Split)

2- Ground applications .at 0.011 lb ai/acre per application, 7 days apart. Concentrations are in μgL^{-1}(ppb)					
Scenario	*Peak*	*96-hr*	*21-day*	*60-day*	***90-day***
Florida (Sweet)	1.85	1.85	1.83	1.8	**1.62**
Florida (Sweet)1	1.19	1.19	1.17	1.12	**0.96**
California	0.56	0.56	0.56	0.55	**0.53**
California1	0.37	0.37	0.36	0.35	**0.34**
Illinois	1.15	1.15	1.48	1.14	**1.13**
Illinois1	0.78	0.77	0.76	0.74	**0.72**
Mississippi	1.31	1.31	1.3	1.28	**1.26**
Mississippi1	0.78	0.78	0.77	0.73	**0.72**
N. Carolina E.	0.64	0.63	0.63	0.62	**0.61**
N. Carolina E.1	0.37	0.37	0.37	0.36	**0.35**
N. Carolina W.	1.15	1.15	1.14	1.13	**1.12**
N. Carolina W.1	0.71	0.71	0.7	0.68	**0.67**
North Dakota	0.75	0.75	0.74	0.73	0.73
North Dakota1	0.47	0.47	0.46	0.44	0.43
Ohio	0.79	0.79	0.78	0.78	0.77
Ohio1	0.55	0.55	0.55	0.54	0.52
Pennsylvania	0.59	0.59	0.59	0.58	0.58
Pennsylvania1	0.35	0.35	0.35	0.34	0.34
Texas	1.24	1.23	1.23	1.21	1.2
Texas1	0.68	0.68	0.67	0.64	0.63

[1] Aerobic aquatic metabolism assumed to be equal to 482.56 days (2 x the aerobic soil metabolism half-life).

The results for aerial and ground applications suggest that it is runoff and not spray drift during application what may be controlling the degree of exposure in an aquatic system. The peak EECs for the Florida corn scenario was 1.73 μgL^{-1} (6.5% less) when the spray drift contribution from two applications was not added to the pond (peak EEC from a single application 1.58 μgL^{-1} with no drift contribution). Drift contributed to as much as 50 percent of the topramezone to the EECs in the California corn scenario, because runoff is quite low since irrigation (corn is apparently not normally irrigated) is not added. However, it should be recognized that the estimates are as good as the quality of environmental fate data used as input parameters. Considering that there are uncertainties about the kinetics and transformation products in water-sediment systems, these estimates carry these uncertainties. The decrease from peak concentration to 90-days is very slight because of the 482.56 day half-life used for aerobic aquatic degradation.

Uncertainties

Several uncertainties (beyond the normal ones, e.g., first order kinetics, validity of Koc model) should be noted for the estimated EECs for topramezone. The first is that the range of soil pH used in the aerobic soil metabolism studies and sorption studies was quite narrow (5.7 to 6.9), the persistence, mobility, and toxicity have been found for other similar chemicals to correlated with pH. A second uncertainty concerns the persistence in the aerobic aquatic environment, as previously discussed under the "Environmental Fate" section. The third uncertainty is the assessment only considers the parent compound[23]. Additional data or information would be needed to improve on these limitations. The petitioner has been requested to address the deficiencies identified in the water-sediment studies.

Model Outputs are contained in Appendix D.

2. Aquatic Exposure Monitoring and Field Data

Topramezone is a new, non-registered chemical. Therefore, no monitoring and field data exist at the time of this assessment. And it is noted that the environmental chemistry method apparently does not have a low enough detection level to measure topramezone at levels potentially hazardous to plants.

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[23] The maximum exposure concentration of metabolites formed in the water column have been estimated as 1.0 μgL^{-1}(ppb) for "M670H10" (anaerobic conditions) and 1.1 μgL^{-1}(ppb) for "M670H01" (aerobic conditions). These estimates were made by multiplying the molecular ratio of each metabolite by the maximum of all of the peak concentrations of parent topramezone (1.2 μgL^{-1}), assuming that all of the topramezone converts completely to "M670H10" or to "M670H01". However, these estimates must be looked at with caution given the uncertainties identified in the biotransformation of topramezone in water-sediment systems. There are no ecotoxicity data for these metabolites.

3. Measures of Terrestrial Exposure

a. Terrestrial Exposure Modeling

Birds and Mammals

Birds and mammals in the field may be exposed to residues of topramezone by incidental ingestion of contaminated soils or drinking water in the treated areas (i.e., oral exposure). Because topramezone is a nonvolatile chemical, inhalation or absorption through the skin are not expected to be significant routes of exposure for birds and mammals.

The estimated environmental concentration (EEC) values used for terrestrial exposure of birds are derived from the Kenega nomograph, as modified by Fletcher *et al.* (1994), based on a large set of actual field residue data. The upper limit values from the nomograph represent the 95th percentile of residue values from actual field measurements (Hoerger and Kenega, 1972). The Fletcher *et al.* (1994) modifications to the Kenaga nomograph are based on measured field residues from 249 published research papers, including information on 118 species of plants, 121 pesticides, and 17 chemical classes. These modifications represent the 95th percentile of the expanded data set. Risk quotients are based on the most sensitive LC50 and NOAEC for birds and LD50 for mammals (based on lab rat studies). These environmental concentration estimates were made with the Terrestrial Exposure Model (TREX), Version 1.1 (October 5, 2004).

The TREX used in estimating environmental concentrations is a spreadsheet based model that calculates the decay of a chemical applied to foliar surfaces for single or multiple applications, assuming first-order decay. In the absence of foliar dissipation data for topramezone, the recommended default value of 35-days was used. For further description of TREX, and outputs refer to Appendix E..

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Estimated Environmental Concentrations (EECs) for Birds and Mammals

Table III.13 Estimated Environmental Concentrations on Avian Food Items (ppm) Following Broadcast Application of Topramezone Products.

Site	App. Rate (lb a.i./acre) / No. of Apps / Intervals	Food Items	EEC Maximum Residue (ppm)	EEC equivalent dose (mg/kg-bw)		
				20 g	100 g	1000 g
Corn	0.022 / 1 application	Short grass	5.28	6	3	2
		Tall grass	2.42	3	2	1
		Broadleaf plants and small insects	2.97	3	2	1
		Fruits, pods, seeds, and large insects	0.33	0	0	0

Table III.14 Estimated Environmental Concentrations on Mammalian Food Items (ppm) Following Broadcast Application of Topramezone Products

Site	App. Rate (lb a.i./acre) / No. of Apps / Intervals	Food Items	EEC Maximum Residue (ppm)	EEC equivalent dose (mg/kg-bw)		
				15 g	35 g	1000 g
CORN	0.022 / 1 application	Short grass	5.28	5	3	1
		Tall grass	2.42	2	2	0
		Broadleaf plants and small insects	2.97	3	2	0
		Fruits, pods, seeds, and large insects	0.33	0	0	0

Non-Target Plant Exposure Modeling

Terrestrial plant exposure characterization employs runoff and spray drift scenarios contained in OPP's TerrPlant model. Exposure calculations are based on the water solubility of a pesticide and the amount of pesticide present on the surface soil within the first inch of depth. For dry areas, the loading of pesticide active ingredient from runoff to an adjacent non-target area is assumed to occur from one acre of treatment to one acre of non-target area. For terrestrial plants inhabiting semi-aquatic (wetland) areas, runoff is considered to occur from a larger source area with active ingredient loading originating from 10 acres of treated area to a single acre of non-target wetland. Default spray drift assumptions are 1% for ground applications and 5% for aerial, airblast, forced air, and chemigation applications.

Estimated Environmental Concentrations for Terrestrial Plants

Table III. 14 Estimated Environmental Concentrations For Dry and Semi- Aquatic Areas (lb ai/A) Following Ground or Aerial Applications (based on 1 application of 0.022 lbs a.i./acre).

Application	**Total Loading to Adjacent Areas (EEC = Sheet Runoff + Drift)**	**Total Loading to Semi-aquatic Area (EEC = Channelized Runoff + Drift)**	**Drift EEC (for ground: application rate x 0.01); (for aerial: application rate x 0.05)**
Ground Unincorporated	0.0013	0.0122	**0.0002**
Aerial, Airblast, Forced-Air and Chemigation	0.0018	0.0077	**0.0011**

b Residue Studies

No foliar dissipation studies are available. Therefore, the recommended default value of 35 days was used in the T-REX Model. This default halflife did not influence the RQs since peak EECs were used.

C. Ecological Effects Characterization

In screening-level ecological risk assessments, "effects characterization" describes the types of effects a pesticide may produce in an organism or plant. This characterization is based on registrant-submitted studies that describe acute and chronic effects toxicity information for various aquatic and terrestrial animals and plants. In addition, other sources of information, including reviews of the open literature, ECOTOX (ECOTOXicity database maintained by EPA's National Health and Environmental Effects Research Laboratory, Mid-Continent Ecology Division) and the Ecological Incident Information System (EIIS), are conducted to further refine the characterization of potential ecological effects. Topramezone is a new active ingredient not registered in the USA. Therefore, a search of the database engines revealed that there are no monitoring, incident data, other sources of information or open literature recorded in the EPA or in other Federal Agency databases that relates to topramezone, except for patent literature and a "Notice of Filing a Pesticide Petition to Establish a Tolerance for a Certain Pesticide Chemical in or on Food" (http://www.epa.gov/fedrgstr/EPA-PEST/2003/June/Day-11/p14328.htm)

This section presents the results of the registrant-submitted toxicity studies used to characterize ecotoxicity effects for this risk assessment. Toxicity testing reported in this section does not represent all species of birds, mammals, aquatic organisms or plants. Only a few surrogate species for both freshwater fish and birds are used to represent all freshwater fish (2000+) and bird (680+) species in the United States. For mammals, acute studies are limited to Norway rat or the house mouse. Estuarine/Marine toxicity testing is limited to a crustacean, a mollusk, and a fish. Also, neither reptiles nor amphibians are tested. The risk assessment assumes that reptiles are not more sensitive than birds and that amphibians are not more sensitive than fish. Only a few dicot and monocot surrogates are used to represent all terrestrial plants. A hazard assessment of the submitted studies can be found in Appendix F.

Summary

As expected for a herbicide, the major effects were on plants. For aquatic plants, toxic effects were higher on vascular than on non-vascular plants. Vascular plants are more sensitive to topramezone (TGAI) than to M670H05 (metabolite) or to BAS 670 00H (formulated topramezone). The most pronounced effects on frond counts were observed for topramezone TGAI. No tests were conducted with "M670H01" or "M670H10", which may exhibit herbicidal activity.

All terrestrial plants showed toxic effects in seedling emergence and vegetative vigor studies, but at varying degree depending on the species and exposure concentrations. In seedling emergence and vegetative vigor studies, monocots were observed to be less sensitive than dicots. The most sensitive plants to seedling emergence were ryegrass (monocot) and cabbage (dicot). The most sensitive plants to vegetative vigor were onion (monocots) and soybeans (dicots). Dry weight was selected as the most sensitive endpoint. However, phytotoxic effects and other growth effects such as shoot height were also observed.

Overall, topramezone is practically nontoxic to avian, mammalians, honeybees, earthworms, freshwater fish and invertebrates and estuarine/marine fish and moderately toxic to estuarine/marine invertebrates. Chronic effects for bobwhite quail reproduction include reduction in the ratio of number hatched to live embryos (a measure of hatchability) at the highest treatment level, 1012 mg ai/kg dw and the mallard duck reproduction had significant reductions in hatchling body weight and female weight gain at all three treatment levels, resulting in the inability to define a NOAEC. No chronic effects were observed in mammals as high as 4000 ppm, based on a two-generation toxicity study on laboratory rats. Chronic effects were apparent for freshwater fish with reduced growth (length and weight) at 9.01 mg aiL^{-1}. Estimated chronic effects for estuarine/marine fish are uncertain because no chronic data were submitted by the registrant; therefore, the NOAEC value was derived based on the assumption that the freshwater and estuarine/marine fish are of equal sensitivity.

M670H05 is practically nontoxic to freshwater fish and invertebrates. The formulated product BAS 670 00H is practically nontoxic to honeybee, terrestrial invertebrates, and freshwater fish and invertebrates.

The reproductive problems seen in chronic toxicity studies do show some effects such as reduction in number hatched to viable embryos, hatchling body weight and female weight gain in birds, thyroid effects for mammals[24], reductions in weight and length of fish and reductions of live offspring produced per female daphnid. This finding would recommend future screening for any endocrine disruption in terrestrial and aquatic animals to better characterize the effects when exposed to topramezone. Disrupting the endocrine system may pose significant risks to animals because proper functioning of the endocrine system is important in regulating growth, development, and reproduction.

> EFED is required under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by Food Quality Protection Act (FQPA), to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EFED determined that there was scientific basis for including, as part of the program, the androgen- and thyroid hormone systems, in addition to the estrogen hormone system. EFED also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

[24] The effects of topramezone on thyroid is related to the metabolism of the chemical in the liver. This chemical induces the liver metabolic enzymes, which in turn causes increased excretion of the thyroid hormone. The decrease of T4 in the blood causes an increase in THS and increase in the size of the thyroid and liver. For topramezone, this leads to thyroid tumors.

In addition, topramezone was found to cause eye effects, pancreatic effects, and skeletal variations typically caused by inhibition of the 4-HPPD enzyme.

1. Aquatic Effects Characterization

a. Aquatic Animals

i. Acute Effects

Freshwater Fish and Aquatic-phase Amphibians

Acute toxicity data are available for parent topramezone, the aerobic soil metabolite "M670H05"[25], and a topramezone formulation (BAS 670 00H; 31% topramezone).

The 96-hour LC_{50} values for the rainbow trout (MRID 45902315) and bluegill sunfish (MRID 45902314) tested with topramezone are in the >97.4 to >100 mg aiL^{-1} (ppm ai) range, topramezone is classified as practically non-toxic to freshwater fish on an acute exposure basis.

No mortality or sublethal effects were observed for the rainbow trout or bluegill. The freshwater fish acute studies are consistent with Guideline §72-1A(a) and §72-1(c) testing requirements and are classified as acceptable. (Table F-10 of Appendix F).

Estuarine/marine Fish

One estuarine/marine fish acute toxicity test using the topramezone (TGAI) was submitted for the preferred test species sheepshead minnow, (*Cyprinodon variegatus*) (MRID 45902319). No mortality or sub-lethal effects were observed in any test or control group following 96 hours of exposure. The resulting LC_{50} of >100 mg aiL^{-1} (ppm ai) categorizes topramezone as practically non-toxic to estuarine/marine fish on an acute exposure basis. The NOAEC was 100 mg aiL^{-1} (ppm ai), the highest concentration tested. This study is classified as acceptable and fulfills guideline requirements for an acute toxicity test with sheepshead minnow (§72-3(a)). The results of this test are provided in **Table F-17** of the Appendix.

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[25] As discussed under "Measures of Aquatic Exposure", "M670H05" was identified only in aerobic soils. It is persistent and very mobile metabolite and it may have potential to accumulate in soils as a result of carryover from season to season. The metabolite "M670H05" can only enter surface water via runoff. "M670H05" was not identified in the biotransformation studies in water-sediment systems. The metabolites that were identified in water-sediment systems are "M670H01 (aerobic conditions) and "M670H10" (anaerobic conditions). Both are potential 4-HPPD inhibitors.

Freshwater Invertebrates

Acute freshwater invertebrate data are available for topramezone, the metabolite M670H05 and the formulated product with the preferred test species, *Daphnia magna*. Results of acute toxicity tests with the daphnid are summarized in **Table F-14 through F-16** of Appendix F.

The 48-hr EC50 value for *D. magna* is >100 mg aiL^{-1} with a NOAEC value of 100 mg aiL^{-1}. (ppm ai) (MRID 45902316). No significant treatment-related effects were seen at the 100 mg aiL^{-1} treatment level, since 5% of daphnids were each immobilized in the controls and the 12.5 mg aiL^{-1} level. Based on the results of this study, topramezone is categorized as practically non-toxic to freshwater invertebrates on an acute exposure basis. The study is scientifically sound, acceptable, and fulfills the §72-2 guideline requirements.

Two studies were submitted on the acute toxicity of the metabolite M670H05 and the formulated product BAS 670 00H to *D. magna* (MRIDs 462427-05 and 459018-20, respectively). No mortality or sublethal effects were seen at the highest concentration group in the studies and are classified as acceptable. The 48-hour EC_{50} values are >100 mg aiL^{-1} (ppm ai) indicates that "M670H05" and the formulated product are practically non-toxic to freshwater invertebrates on an acute exposure basis. Both studies are scientifically sound, acceptable, and satisfy the §72-2 guideline requirements.

Estuarine/marine Invertebrates

Acute topramezone toxicity data are available for mysid shrimp (*Americamysis bahia*) and the Eastern oyster (*Crassostrea virginica*), and the results are summarized in Table F-18 of Appendix F. Results indicate that shrimp was more sensitive to topramezone than the oyster.

The 96-hour mysid shrimp EC_{50} is 2.7 mg aiL^{-1} (MRID 4590238); therefore, topramezone is classified as moderately toxic to saltwater crustaceans on an acute exposure basis. After 96 hours, mortality in the 1.3, 2.6, and 5.1 mg aiL^{-1} (ppm ai) treatment groups was 5, 55, and 85%, respectively. One mortality (5%) had occurred in the control group. No sublethal effects were seen in all treatment groups and controls, the NOAEC was 1.3 mg aiL^{-1} (ppm ai). A dose-response relationship was evident. The slope of the dose response curve with 95% confidence intervals was 4.5 (95% C.I.: 2.76 - 6.14). The study is scientifically sound, acceptable, and fulfills §72-3(c) guideline requirements for an acute toxicity test with mysid shrimp.

b. Chronic Effects

The only data available to evaluate chronic effects on aquatic animals is an early life-stage toxicity test conducted with the freshwater fish, rainbow trout. No data are available to evaluate chronic effects on estuarine/marine fish or freshwater and estuarine/marine invertebrates, although there is an assumption that freshwater and estuarine/marine fish are of equal sensitivity.

Freshwater Fish

A freshwater fish early life-stage test using technical grade topramezone (TGAI) was submitted (MRID 45902321) using the preferred test species, rainbow trout. No treatment-related effects on hatchability and survival parameters were observed. The survival rate in the viability control (mean of 100 embryos) after 14 days was 83%. Survival at the termination of the hatching period (Day 35) was 91% (criteria: >66%) relative to total numbers of fertilized eggs, or 110% relative to the percentage of fertilized eggs seen in the viability controls. Mean survival at test termination (Day 96) was 99% relative to Day 55 survivors, and 70% relative to Day 35 survivors (criteria ≥70%).

Treatment-related effects on growth (length and weight) were observed to be significant. Sublethal effects caused by BAS 670 H were observed in the 9.01 mg aiL^{-1} treatment. Fish in the juvenile stage (day 55-96) in the highest concentration group, 9.01 mg aiL^{-1} , treatment showed a reduction in body length. These observations were confirmed by the significant differences observed in total length and wet weight between the fish in this treatment and the control fish. The total mean wet weight of the surviving fish at study termination was significantly lower in the 9.01 mg aiL^{-1} treatment compared to the control. Similarly, the total mean body length of the surviving fish on day 96 was significantly lower in the 9.01 mg aiL^{-1} treatment compared to the control. A significant difference in mean length was observed between the fish in the 0.90 mg aiL^{-1} and the control fish; however, the effect was opposite to the one expected: fish in the 0.90 mg aiL^{-1} treatment were significantly longer than the control fish. This may have been caused by the fewer number of survivors in this group, leading to a lower loading of the test vessel. This is not considered to be a substance-related effect. No significant difference in the mean body length was observed between the control fish and those in the 2.93 mg aiL^{-1} treatment. As a result, the NOAEC values, based on mortality of juveniles (day 55 to day 96) and reproductive effects, are both 2.93 mg aiL^{-1} treatment, in which reduced activity was seen occasionally in a higher proportion of the trout

Shortly after the end of hatch and until study day 58, sporadic abnormalities in single trouts were observed in all the 4 replicates of the control group, such as reduced activity, apathy and decreased respiration rate. Abnormalities in the concentration groups were comparable to the control group and were observed only in a few individuals with the exception of the 9.01 mg aiL^{-1}

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during the last two weeks of study, and in which fish growth was clearly reduced, showing a clear reduction in body length while body width appeared normal. The abundance of deformations was not increased markedly in the concentration groups. At study termination, deformations were observed in one individual from the 0.10 mg aiL^{-1} treatment. No deformations were observed in the control fish. Two trouts with deformations were observed in the 9.01 mg aiL^{-1} treatment, but likely did not survive until the end of the study.

The study is classified as acceptable and fulfills the §72-4 guideline requirements. The results are summarized in **Table F-13** of Appendix F.

Estuarine/Marine Fish

No data were available to assess the chronic toxicity of topramezone to estuarine/marine fish. An estimated NOAEC value of 2.93 mg aiL^{-1} (ppm ai) was derived for estuarine/marine fish based on the assumption that the freshwater and estuarine/marine fish are of equal sensitivity. This assumption was based on the sensitivity of both fish seen in the acute toxicity tests though the LC_{50} values of >100 mg aiL^{-1} were not discrete. Extrapolation from freshwater to estuarine/marine chronic NOAEC values is possible; however, there is uncertainty associated with this assumption because quantifiable taxonomic sensitivity factors between the two broad categories of fish do not exist.

There is additional uncertainty associated with the estimated chronic NOAEC for estuarine/marine fish because the acute toxicity data do not allow for a determination of the relative sensitivity of freshwater and estuarine/marine fish.

Freshwater Invertebrates

The 21-day-chronic toxicity of BAS 670 H to *Daphnia magna* (MRID 45902320) was studied under semi-static conditions. Ten replicates of 1 adult female were exposed to control, and topramezone at mean measured test concentrations were <0.06 (<LOQ, control), 6.1, 12.3, 25.1, 48.6, and 97.5 mg aiL^{-1} . Parameters measured included survival of first generation daphnids, mean number of live offspring produced per female daphnid, and number of aborted subitane eggs per surviving female. Dry weight of surviving daphnids were not measured.

The 21-day EC_{50} based on mortality/sublethal effect was >97.5 mg aiL^{-1} . The 21-day NOAEC and LOAEC based on reduced mean number of live offspring produced per female daphnid, was 48.6 and 97.5 mg aiL^{-1} , respectively. Production of offsprings in the treated groups indicated that BAS 670 H had an effect on the reproduction at concentrations greater than 48.6 mg aiL^{-1} . The most sensitive end point was reproduction.

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This study is classified as scientifically sound but does not fulfills the data requirement for an *Daphnia magna* reproduction test guidelines. The Agency has classified this study as supplemental.

b. Aquatic Plants

Toxicity data for topramezone is available for both vascular and non-vascular plants. Data on the metabolite M670H05 and the formulated product is available only for vascular plants. A summary of Tier II toxicity of topramezone, M670H05, and product to vascular aquatic plants is provided in **Table F-21 through F-23** of Appendix F. A summary of Tier II toxicity of topramezone to non-vascular aquatic plants is also provided in **Table F-21** of Appendix F.

Vascular Plants

Three Tier II toxicity studies for vascular plants, using duckweed (*Lemna gibba*) as the surrogate species, were conducted with topramezone TGAI, the metabolite M670H05[26] and formulated topramezone as test substances. Results indicate that vascular plants are more sensitive to topramezone TGAI than to M670H05 or formulated topramezone. Note that the most pronounced effects on frond counts were observed for topramezone TGAI.

Tier II study of the freshwater aquatic vascular plant, duckweed (*Lemna gibba*), was completed using the TGAI of topramezone. In this study (MRID 459023-29), frond number was the most sensitive endpoint with the EC_{50} value at 8 µg aiL^{-1} (ppb ai); the NOAEC and EC_{10} values were 1 and 1.8 µg aiL^{-1} (ppb ai), respectively. The % inhibition of frond numbers in the treated cultures compared to the control ranged from -2.5 to 66.9%, respectively. Abnormalities of small frond size and discoloration (chlorotic, brown or white) of new fronds were noted. This study is scientifically sound and satisfies the U.S. EPA Guideline Subdivision J, §123-2 for aquatic vascular plant studies with *L. gibba*. This study is classified as acceptable.

A Tier II test of the vascular plant, duckweed (*Lemna gibba*) was also completed for the metabolite M670H05 (MRID 462427-04). The results of this study show frond number and average 0-7 day growth rate were significantly reduced by exposure to M670H05. The % inhibition in frond numbers and in specific growth rate in the treated cultures as compared to the control ranged from 4.5 to 62% and from 1.5 to 30.4%, respectively. No effects on frond appearance were observed throughout the study. The most sensitive endpoint was frond number, with a 7 day NOAEC, EC_{10} and EC_{50} value of 6.7 µg M670H05 L^{-1}, 10 µg M670H05 L^{-1} and 360 µg M670H05 L^{-1} (ppb ai), respectively. The Tier II study on the metabolite M670H05 is

[26] As indicated earlier, "M670H05" was only found in the aerobic soil metabolism study. This metabolite could enter surface water by runoff, but not by drift.

scientifically sound, satisfy the U.S. EPA Guideline Subdivision J, §123-2 for an aquatic vascular plant study with *L. gibba* and is classified as acceptable.

A Tier II test of the vascular plant, duckweed (*Lemna gibba*) was also completed for the formulated product BAS670 00H (MRID 45901821). The results of this study show frond number and average 0-7 day growth rate were significantly reduced by exposure to BAS 670 00 H. The % inhibition in frond numbers and in specific growth rate in the treated cultures as compared to the control ranged from -3.2 to 67% and from -1.3 to 38.6%, respectively. Abnormalities of single fronds, small frond size and discoloration (chlorosis) of new fronds were noted. The most sensitive endpoint was frond number, with a 7 day NOAEC, EC_{10} and EC_{50} value of 2.3 µg EP L^{-1}, 3.1 µg EP L^{-1} and 28.6 µg EP L^{-1}, respectively. The Tier II study on the metabolite M670H05 is scientifically sound, satisfy the U.S. EPA Guideline Subdivision J, §123-2 for an aquatic vascular plant study with *L. gibba* and is classified as acceptable.

Non-vascular Plants

Four Tier II, 96-hour exposures, studies were completed using four non-vascular plant surrogates and parent topramezone (topramezone TGAI). The non-vascular plant surrogates included *Navicula pelliculosa* (freshwater diatom), *Skeletonema costatum* (marine diatom), and the green algae *Anabaena flos-aquae* and *Pseudokirchneriella subcapitata.*

Cell density (biomass) was identified as the most sensitive endpoint. Of all the non-vascular surrogates tested, the green algae *Pseudokirchneriella subcapitata* was the most sensitive species.

In the test with *A. flos-aquae* (MRID 45902330), after 96 hours of exposure to BAS670H, the growth rate of *A. flos-aquae* was reduced by 0.2 - 6.9%, and biomass was reduced by -4.1(i.e., stimulated) to 15.6% relative to controls. A clear dose-response relationship was not evident for either endpoints examined, with maximum inhibition occurring at 56 mg a.i.L^{-1}. No morphological effects on the algae were observed. The most sensitive endpoint was biomass, with NOAEC, EC_{10} and EC_{50} value of 32 mg ai L^{-1}, >100 mg ai L^{-1} and >100 mg ai L^{-1}, respectively. The Tier II study is scientifically sound, satisfy the US EPA Guideline Subdivision J, §123-2 for a freshwater blue-green algae study with *A. flos-aquae* is classified as acceptable.

In the test with *S. costatum* (MRID 459023-31), results show after 96 hours of exposure to BAS 670 H, cell densities were reduced by 8.9 - 56% relative to controls. A clear dose-response relationship was evident, with statistical significance at the ≥6.0 mg a.i. L^{-1} concentrations. No morphological effects on the algae were observed. The most sensitive endpoint was cell densities, with a NOAEC and EC_{50} value of 3 mg ai L^{-1} and 49 mg ai L^{-1}, respectively. The Tier II study is scientifically sound, satisfy the U.S. EPA Guideline Subdivision J, §123-2 for a marine algal (nonvascular) study with *S. costatum* is classified as acceptable.

In the test with *P. subcapitata* (MRID 459023-33), results show after 96 hours of exposure to BAS 670 H, the growth rate was reduced by 2.0 - 61.3%, and biomass was reduced by 8.2 - 93.8% relative to controls. A clear dose-response relationship was evident for both endpoints examined. No morphological effects on the algae were observed. The most sensitive endpoint was biomass, with NOAEC, EC_{10} and EC_{50} value of 3 mg ai L^{-1}, 17 mg ai L^{-1} and 17.2 mg a.i L^{-1}, respectively. The Tier II study is scientifically sound, satisfy the US EPA Guideline Subdivision J, ∲ 123-2 for a freshwater green algae study with *P. subcapitata* is classified as acceptable.

2. Terrestrial Effects Characterization

a. Terrestrial Animals

i. Acute and Subacute Effects

Birds

Topramezone is classified as practically non toxic to birds on an acute exposure basis. Topramezone is practically non-toxic to the bobwhite quail *(Colinus virginianus)* and the mallard duck *(Anas platyrhnchos)* on a subacute dietary basis. A summary of acute and subacute toxicity of topramezone to birds is provided in **Tables F-1 and F-2** of Appendix F.

The acute oral toxicity of topramezone to 13-month old bobwhite quail (*Colinus virginianus*) was assessed over 14 days (MRID 45902309). The 14-day acute oral LD_{50} exceeded the highest dose tested (>2000 mg a.i./kg bw), **Table F-1** of Appendix F. There was no mortality during the study. No phyisological or behavioral abnormalities were observed and body weights and food consumption remained unaltered. According to the U.S. EPA classification, topramezone is classified as practically non-toxic to birds on an acute exposure basis. The study is scientifically sound, satisfy the §71-1 US EPA guideline requirement for an avian oral study with bobwhite quail is classified as acceptable.

Two subacute dietary studies using the active ingredient are required to establish the toxicity of topramezone to birds. The results of the dietary studies for the preferred test species, 11-day old bobwhite quail (*C. virginianus*) and 8-day old mallard duck (*Anas platyrhynchos*), are summarized in **Table F-2** of the Appendix In the 8-day quail study (MRID 45902310), no mortality occurred in any control or test group, and no clinical signs of toxicity or abnormalities upon necropsy were observed. The LC_{50} exceeded the highest test concentration, >5000 mg a.i/kg dw (ppm a.i.), which categorizes topramezone as practically non-toxic to the bobwhite quail on an acute dietary basis. The NOAEC was determined to be 5000 mg ai/kg dw (ppm ai). This quail study is scientifically sound, but does not fulfill the guideline requirements for an avian subacute dietary study using the Northern Bobwhite quail (§71-2a) because data verifying the stability of the test substance in treated feed were not provided. This study is classified as supplemental.

In the 8-day mallard study (MRID 45902311). no mortality was observed in any control or test group, and no clinical signs of toxicity were observed. The LC_{50} exceeded the highest test concentration, >5000 mg ai/kg dw (ppm a.i.), which categorizes topramezone as practically non-toxic to the mallard duck on an acute dietary basis. The NOAEC was determined to be 5000 mg ai/kg dw (ppm ai). This duck study is scientifically sound and satisfies the guideline requirement for subacute dietary study for mallard duck, and is classified as acceptable.

Mammals

Three acute mammalian studies (summarized in **Table F-4** of Appendix F) were submitted and considered in this assessment. Rats exposed to technical grade topramezone showed no mortality, clinical signs, or gross lesions at the highest doses tested. All rats gained weight during the study. Corresponding LD_{50} values for the 3 studies are >2000; classifying topramezone as practically non-toxic to mammals on an acute basis (MRID 45902118, 45902119, and 45902120).

Terrestrial-phase Amphibians, Reptiles, and Beneficial Insects (Honey Bee)

The acute contact toxicity to honeybees (*Apis mellifera*) was tested for topramezone active ingredient and the acute contact and oral toxicity was tested with the formulated product (48 hours). Topramezone and the tested formulated product are categorized as practically non-toxic to honeybees on an acute contact and oral basis. The LD_{50} for both topramezone and the formulated product were > 100 µg a.i./bee for the contact and oral tests (MRID 45901819 and 45902325). For further information refer to **Tables F-6 and F-7** of Appendix.F.

Earthworms and other Terrestrial Invertebrates

Acute toxicity studies to earthworms (*Eisenia foetida*) and other terrestrial invertebrates (parasitic wasp, *Aphidius rhopalosiphi*; predator lacewing, *Chrysoperla carnea*; carabid beetle, *Poecilus cupreus*; predatory mite, *typhlodromus pyri*) in accordance with OECD guidelines, were performed for the active ingredient topramezone and its formulated product. As shown in **Tables F-8 and F-9** of the Appendix, acute LC_{50} values for both topramezone and BAS670 00H formulation are greater than the highest treatment level tested. No significant mortality and/or sublethal effects were observed in any of the treatment groups. All of the terrestrial invertebrate toxicity studies are classified as supplemental, because these types of tests are not required by the Agency for pesticide registration.

ii. Chronic Effects to Terrestrial Animals

Birds

Two studies were submitted. One of the studies was conducted with the bobwhite quail (*Colinus virginianus*; MRID 45902312; Data Requirement Guideline §71-4a) and the other with the mallard duck (*Anas platyrhynchos*; MRID 45902313; Data Requirement Guideline §71-4b), but in both of the studies the stability of the test substance (topramezone) in the treated feed was not reported. Results are summarized in **Table F-3** of the Appendix.

Bobwhite Quail

The one generation reproductive toxicity to groups of 16 pairs of 6-month-old bobwhite quail (*Colinus virginianus*) was assessed over 22 weeks. No significant treatment-related effects were seen on mortality, egg production, egg weight, eggshell thickness, fertility rates of eggs, or sublethal effects. There was a reduction (p-value = 0.017) in the ratio of number hatched to live embryos (a measure of hatchability) at the highest treatment level, 1012 mg ai/kg dw. Chick survival 14-days after hatch was not significantly affected by exposure to topramezone at doses up to 1012 mg a.i./kg dw (ppm a.i.) diet. There was no evidence of test substance-effects on body weights of hatchlings or 14-days old survivors. The adult birds may have exhibited a minor avoidance of treated diet, as there was a slight increasing trend in feed consumption with treatment level which may have been due to spillage. Food consumption throughout weeks 1 - 22 showed a slight dose-related trend, with rates being 4.0, 5.3 and 8.0% higher than controls at 100, 300 and 1000 mg a.i./kg (ppm) diet, respectively. There were significant increases in food consumption relative to controls at all treatment levels for some individual weeks over the study, however, the 8.0% increase at 1000 mg a.i./kg (ppm) diet was not considered to be biologically relevant. Although the authors report no marked rejection of feed containing topramezone, the slight increase in food consumption with dose may be a result of increased spillage due to changing taste of the diet containing topramezone.

The NOAEC and LOAEC of topramezone to the bobwhite quail based on the reproductive parameters was 294 and 1012 mg ai/kg dw (ppm a.i.) diet, respectively. when compared to the control. The stability of the topramezone in the treated feed was not assessed at concentration levels relevant to the definitive test.

Mallard Duck

In the mallard duck one-generation reproduction study to groups of 16 pairs of mallard ducks (approximately 5-months-old) per treatment group was assessed over 22 weeks. The analysis revealed statistically significant reductions in hatchling body weight (p-value = 0.006) and female weight gain (p-value = 0.021) at all three treatment levels, resulting in the inability to define a NOAEC in this study (<100 mg a.i./kg dw (ppm a.i.) diet). The LOAEC based on reductions in body weight was determined to be 100 mg a.i./kg diet, the lowest concentration tested. No topramezone-related effects were observed on any other adult or offspring parameter. The stability of the topramezone in the treated feed was not assessed and a NOAEC could not be determined. If multiple applications or a higher application rate of topramezone is requested in the future, this study will be required to be repeated using lower test concentrations and with data verifying the stability of topramezone under actual use conditions.

Mammals

In a two-generation reproduction toxicity study (MRID 45902214), laboratory rats exposed to technical grade topramezone showed no treatment-related effects on: mortality, estrous cycle, sperm enumeration, morphology, or motility; pre-coital or gestation intervals; number of implantations; post-implantation loss; or mating, fertility, gestation, or live birth indices. With no treatment-related effects, the NOAEC and LOAEC were 4000 and >4000 ppm ai (equivalent to 426.8/471.9 mg ai/kg/day for males and females), respectively (see **Table F-5** of the Appendix).

b. Terrestrial Plants

Like data for vascular and non-vascular plants, data from Tier II terrestrial plant testing are critical in evaluating the risk of herbicides to non-target plants.

Toxicity data for BAS670 00H formulation (31% active ingredient; proposed product is 29.7%) is available for both seedlings and grown plants exposed at a single application up to 50 g/ha (0.045 lb ai/A). This rate is more than 2x higher than the maximum application rate of 0.022 lbs ai/acre proposed for topramezone. In addition, data for BAS670 00H formulation plus an adjuvant is available for peas exposed at an application up to 0.1005 lb BAS 670 00H/A + 0.4465 lb DASH HC/A under field conditions.

Seedling Emergence

An acceptable 21-day Tier II study of the seedling emergence (MRID 459023-27) with 10 terrestrial plant species (bean (*Phaseolus vulgaris*), cabbage (*Brassica oleracea*), lettuce (*Lactuca sativa*), radish, (*Raphanus sativus*), soybean (*Glycine max*), tomato (*Lycopersicon escuylentum*), onion (*Allium cepa*), corn (*Zea mays*), ryegrass (*Lolium perenne*) and wheat (*Triticum aestivum*)) were studied at the seed stage. After 21-days, emerged seedlings were evaluated for phytotoxicity, percent emergence. and percent reduction in shoot length or shoot weight.

Plant emergence rates by Day 21 were >85% for all species. The observed NOAEC for % emergence was 0.045 lb/A for all species. The most sensitive dicot was cabbage, with a NOAEC of 0.0017 lb/A and EC_{25} of 0.0039 lb/A for dry weight. The most sensitive monocot was ryegrass, with a NOAEC of 0.015 lb/A and EC_{25} of 0.042 lb/A for dry weight.

The condition of surviving seedlings (**Table III.13**) appeared normal in the control and the 0.00019, 0.0006, and 0.0017 lb/A groups, but several seedlings in the 0.005, 0.015 and 0.045 lb/A groups showed increased evidence of phytotoxicity including necrosis, chlorosis and leaf curl. Monocots were observed to be less sensitive to topramezone than dicots. Further details are included in **Tables F-19 and F-19a** of Appendix F.

Table.III.15 Condition (Phytotoxicity) of Surviving Seedlings

Plant Injury Index at 17 g ai/ha or 0.015 lb ai/A *									
Soybean	Lettuce	Radish	Tomato	Bean	Cabbage	Wheat	Ryegrass	Corn	Onion
4-12% LC, CL	13-49% CL, N	33-63% LC, CL, N	22-65% N	n/a	20-65% LC, CL, N	n/a	2-13% CL, N	n/a	0-6% N

* 0% = No effect; 10% = Effect barely noticeable; 20% = Some effect, not apparently detrimental; 30% = Effect more pronounced, not obviously detrimental; 40% = Effect moderate, plants appear able to recover; 50% = More lasting effect, recovery doubtful; 60% = Lasting effect, recovery doubtful; 70% = Heavy injury, loss of individual leaves; 80% = Plant nearly destroyed, a few surviving leaves; 90% = Occasional surviving leaves; 100% = plant death. CL = Chlorosis; LC = Leaf Curl; N = Necrosis; S = Stunting; D = mildew

The conditions of surviving seedlings at the observed application of 0.015 lb/A show bean, corn, and wheat were generally normal and not effected. Soybean, ryegrass, onion, and lettuce were moderately affected with an increase in phytotoxicity of chlorosis. leaf curl and necrosis observed but appears to recover back to normal levels. Radish, tomato and cabbage were detrimentally effected with a pronounce increase in phytotoxicity of chlorosis, leaf curl and necrosis.

Vegetative Vigor

An acceptable 21-day Tier II study of the vegetative vigor (MRID 45902328) with 10 terrestrial plant species (bean (*Phaseolus vulgaris*), cabbage (*Brassica oleracea*), lettuce (*Lactuca sativa*), radish, (*Raphanus sativus*), soybean (*Glycine max*), tomato (*Lycopersicon escuylentum*), onion (*Allium cepa*), corn (*Zea mays*), ryegrass (*Lolium perenne*) and wheat (*Triticum aestivum*) were studied at the 1-2 true leaf stage.

After 21-days, growing plants were evaluated for phytotoxicity and percent reduction in shoot length or shoot weight. Based on results, the most sensitive monocot was onion with a NOAEC of 0.005 lb/A and an EC_{25} of 0.0098 lb/A, based on dry weight. The most sensitive dicot was the soybean with an EC_{05} of 0.000009 lb/A, an EC_{25} of 0.0001 lb/A, based on dry weight.

The condition of growing plants appeared normal in both the negative and adjuvant control groups. There was increased evidence of phytotoxicity (**Table III.14**) including necrosis, chlorosis, leaf curl and wilting with increasing test concentrations for all dicots tested. Visible effects were less severe for the monocots. See also **Tables F-20 and F-20a** of Appendix F.

Table III.16. Condition (Phytotoxicity) of Growing Plants

Plant Injury Index at 17 g ai/ha or 0.015 lb ai/A*									
Soybean	Lettuce	Radish	Tomato	Bean	Cabbage	Wheat	Ryegrass	Corn	Onion
82-90% LC, N	100% S, N	90-100% CL, LC, N	90-94% CL, LC, N, S	28-64% N	96-100% LC, N	4-14% CL, LC, N, D	0-3% N	0%	0-6% N

* 0% = No effect; 10% = Effect barely noticeable; 20% = Some effect, not apparently detrimental; 30% = Effect more pronounced, not obviously detrimental; 40% = Effect moderate, plants appear able to recover; 50% = More lasting effect, recovery doubtful: 60% = Lasting effect, recovery doubtful; 70% = Heavy injury, loss of individual leaves; 80% = Plant nearly destroyed, a few surviving leaves; 90% = Occasional surviving leaves; 100% = plant death. CL = Chlorosis; LC = Leaf Curl; N = Necrosis; S = Stunting; D = mildew

The conditions of growing plants at the observed application of 0.015 lb/A show corn, onion and ryegrass were generally normal and not effected. Wheat appears to be normal with a slight increase of chlorosis, leaf curl, necrosis and mildew. Bean was detrimentally effected with a pronounce increase in phytotoxicity of necrosis. Soybean, lettuce, radish, tomato and cabbage were nearly destroyed with some approaching death and a pronounce increase in phytotoxicity of leaf curl, chlorosis, necrosis and stunting.

Field Study

A vegetative vigor field study was submitted (MRID 46460702) to observe the effect of topramezone's formulated product BAS670 00H including an adjuvant (DASH HC) to pea under field conditions. Results indicate that the response of pea plants from treatment conditions did not differ from control plants with the exception of the two highest treatment levels (0.5 + 0.2233 and 0.1005 lb BAS 670 00H/A + 0.4465 lb DASH HC/A). The phytotoxic effects in the 0.5 + 0.2233 and 0.1005 lb BAS 670 00H/A + 0.4465 lb DASH HC/A were 33 and 85%, respectively. The EC25 was determined to be 0.048 lb BAS 670 00H/A + 0.22 lb DASH HC/A. The NOAEC was 0.025 lb BAS 670 00H./A + 0.1116 lb DASH HC/A. The study is classified as supplemental because it is unknown whether the effects were caused by the adjuvant or the end use product. A solvent control for the adjuvant DASH HC was not tested. In addition, there was no indication whether the control plots were separated from treated plot to prevent cross-contamination between plots.

Summary of Toxicity Data for Plant Studies (Aquatic and Terrestrial)

The toxicity data for all of the plant studies (**Tables III.17 through III.19**) are summarized below. These data were the basis for selecting the endpoints and other necessary information for the plant risk assessment.

Table III.17. Summary of Aquatic Plant Toxicity Data for Topramezone

Species	% ai	EC_{50}, mg aiL^{-1}	NOAEC, mg aiL^{-1}	MRID no.	Study classification
Nontarget Aquatic Plant Toxicity (Tier II)					
Vascular species:					
Duckweed (*Lemna gibba*)	95.8	0.008	0.001	45902329	Acceptable
Nonvascular species:					
Anabaena flos-aquae	95.8	>100	100	45902330	Acceptable
Skeletonema costatum	95.8	49	3	45902331	Acceptable
Pseudokirchneriella subcapitata.	95.8	17	3	45902333	Acceptable

Table III.18. Summary of Seedling Emergence Toxicity Data Based on Dry Weight for Topramezone (As a formulated product)

Nontarget Terrestrial Plant Seedling Emergence Toxicity (Tier II) [1]

Species	% ai	EC_{25} (lb/A)	NOAEC (lb/A)	Endpoint Affected[2]	Slope
	31				
Dicot-Cabbage		0.0039	0.002	dry weight	1.44
Dicot- Lettuce		0.007	0.005	dry weight	1.72
Dicot-Radish		0.009	0.005	dry weight	2.82
Dicot-Tomato		0.044	0.015	dry weight	1.21
Dicot-Soybean		>0 045	0.045	none	n/a
Dicot- Bean		>0.045	0.045	none	n/a
Monocot- Ryegrass		0.042	0.015	dry weight	2.68
Monocot- Onion		>0.045	0.045	none	n/a
Monocot- Corn		>0.045	0.045	none	n/a
Monocot- Wheat		>0 045	0.045	none	n/a

1 MRID no. 459023-27; proposed label application rate is 0.022 lb ai/A, however, test was conducted at 0.045 lb ai/A (2x max. appl. rate).

2 only the most sensitive endpoint is tabulated, if no effects are observed a "none" is denoted.

Table III.19 Summary of Vegetative Vigor Toxicity Data Based on Dry Weight for Topramezone (As a formulated product)

Nontarget Terrestrial Plant Vegetative Vigor Toxicity (Tier II)1

Species	% ai	EC_{25} (lb/A)	NOAEC (lb/A)	Endpoint Affected2	Slope
	31				
Dicot-Soybean		0.0001	[0.000009]A	dry weight	0.893
Dicot- Cabbage		0.0005	[0.00015]	dry weight	1.92
Dicot- Tomato		0 0005	0.0002	dry weight	1.73
Dicot-Radish		0 0008	0.0006	dry weight	1.17
Dicot- Lettuce		0.001	0.0002	dry weight	3.64
Dicot- Bean		0.002	[0.0004]	dry weight	1.5
Monocot- Onion		0 01	0.005	dry weight	1.02
Monocot- Wheat		0.029	0.015	dry weight	2.56
Monocot- Ryegrass		>0 034	0.034	none	n/a
Monocot- Corn		>0.045	0.045	none	n/a

A [EC05]

1 MRID no. 459023-28; proposed label application rate is 25 g ai/A, however, test was conducted at 50 g ai/A (2x max. appl. rate).

2 only the most sensitive endpoint is tabulated

Table III.20 Summary of Toxicity Data for Wildlife Studies (Aquatic and Terrestrial)

Species	Acute Toxicity			Chronic Toxicity	
	96-hr LC_{50}, mg L^{-1}	48-hr EC_{50}, mg L^{-1}	Acute Toxicity	NOAEC / LOAEC mg L^{-1}	Affected Endpoints
Rainbow Trout *Oncorhynchus mykiss* (TGAI)	>97.4	-	practically nontoxic	2.93 / 9.01	wet weight, length, juvenile survival; abnormalities included decreased growth (reduction of body length) in juveniles.
Bluegill sunfish *Lepomis macrochirus* (TGAI)	>100	–	practically nontoxic	--	--
Rainbow Trout *Oncorhynchus mykiss* (metabolite)	>100	–	practically non-toxic	--	--
Rainbow Trout *Oncorhynchus mykiss* (formulation)	>100	--	practically nontoxic	--	--
Water flea *Daphnia magna* (TGAI)	–	>100	practically nontoxic	50 / 100	mean number of live offspring produced per female daphnid
Water flea *Daphnia magna* (metabolite)	–	>100	practically nontoxic	–	–
Water flea *Daphnia magna* (formulation)	--	>100	practically nontoxic	--	--
Sheepshead minnow *Cyprinodon variegatus* (TGAI)	>119	–	practically nontoxic	–	--
Eastern oyster *Crassostrea virginica* (TGAI)	>123	–	practically nontoxic	–	--
Mysid shrimp *Americamysis bahia* (TGAI)	2.7	–	moderately toxic	--	--

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Species	Acute Toxicity				Chronic Toxicity	
	LD_{50} (ppm)	Acute Oral Toxicity	5-day LC_{50} (ppm)	Subacute Dietary Toxicity	NOAEC / LOAEC (ppm)	Affected Endpoints
bobwhite quail *Colinus virginianus*	>2000	practically non-toxic (458654-22)	>5000	practically nontoxic	294 / 1012	reproduction
Mallard duck *Anas platyrhynchos*	--	--	>5000	practically non-toxic	<100 / 100	growth
Honey bee *Apis meliferus*	>100 (µg/bee contact)	practically non-toxic	-	-	-	-
Laboratory rat *Rattus norvegicus* (TGAI)	>2000	practically non-toxic	--	-	4000 / >4000	no effects

Selection of Endpoints for Risk Quotient Calculations for Plants

Tables III.21 through III.24 summarize the selections to estimate Risk Quotients for the non-target plant risk assessment.

Table III.21. Aquatic Plants (Topramezone)

Surrogate Species	EC_{50}, mg aiL^{-1}	NOAEC mg aiL^{-1}	Endpoint
Vascular Plants, Duckweed *Lemna gibba*	0.008	0.001	Biomass Reduction
Non-vascular Plants, Green Algae *Pseudokirchneriella subcapitata.*	17	3	Biomass Reduction

Table III.22 Terrestrial Plants , Seedling Emergence (at 21 days); Topramezone as a Formulated product

Surrogate Species	NOAEC, lbs/A	EC_{25} lbs/A	End-point
Monocot (Ryegrass)	0.015	0.042	Dry weight
Dicot (Cabbage)	0.0017	0.0039	Dry weight

Table III.23 Terrestrial Plants , Vegetative Vigor (at 21 days); Topramezone as a Formulated product

Surrogate Species	NOAEC, (lbs/A)	EC_{25} (lbs/A)	End-point
Monocot (Onion)	0.005	0.0098	Dry weight
Dicot (Soybean)	[0.000009][1]	0.0001	Dry weight

[1]Use as EC05 because the NOEC value is above the EC25

Table III. 24 **Wildlife Animals (Topramezone)**

Surrogate Species	NOAEC	LC_{50} or LOAEC	End-point
Freshwater Fish Acute (Trout) LC50, mgL^{-1}	97.4	>97.4	No effect
Freshwater Invertebrate Acute (daphnid) EC50, mgL^{-1}	100	>100	No effect
Freshwater Fish Chronic (Trout) NOAEC, mgL^{-1}	2.93	9.01	wet weight, length, juvenile survival; abnormalities included decreased growth (reduction of body length) in juveniles.
Freshwater Invertebrates Chronic (daphnid) NOAEC, mgL^{-1}	48.6	97.5	mean number of live offspring produced per female daphnid
Estuarine/marine Fish Acute (sheepshead minnow) LC50, mgL^{-1}	119	>119	No effect
Estuarine/marine Invertebrate Acute (mysid shrimp) EC50, mgL^{-1}	--	2.7	Survival
Avian Oral Acute (Northern bobwhite quail) LD50, ppm	2000	>2000	No effects
Avian Dietary Subacute (Northern bobwhite quail) LC50, ppm	5000	>5000	No effects
Avian Reproduction (Mallard duck) NOAEC, ppm	<100	100	Hatchling body weight and adult female weight gain
Mammalian Oral Acute (laboratory rat) LD50, ppm	2000	>2000	No effects
Mammalian Reproduction NOAEC, ppm	4000	>4000	No effects

IV. Risk Characterization

Risk characterization integrates exposure and effects characterizations to provide an estimate of risk (RQ, Risk Quotient = Exposure/Toxicity) relative to Levels of Concerns (LOCs.) established by the Agency. It also includes a risk description which is an interpretation of the risk estimates.

A. Risk Estimation - Integration of Exposure and Effects Data

In this deterministic approach, a single point estimate of toxicity is divided by an exposure estimate to calculate a risk quotient (RQ). The RQ is then compared to Agency LOC's that serve as criteria for categorizing potential risk to non-target organisms. A description of the Risk Presumptions for terrestrial, aquatic animals and plants can be found in appendix G.

1. Non-target Terrestrial Animals

Birds

Exposure to birds and mammals for Tier 1 assessments is based on the upper 95th percentile residues on food items from collections of field residues on various plant types as reported by (Hoerger, F. and E.E. Kenaga, 1972) and further supported by additional analysis reported in Fletcher et al. (1994). The upper 95th percentile EECs on short grass is ~5-6 mg ai/kg food at 0.022 lb ai/acre. These are substantially lower than the results of the dietary LC_{50} studies for both mallard and bobwhite which are both >5000 mg ai/kg food. The RQs for acute toxicity to birds are not being calculated because the LC_{50}s are > 5000 mg ai/kg food. It is unlikely that such concentration of topramezone would be found in the environment.

Chronic RQ for the Mallard duck are in Table IV.1. Normally, the NOAEC is used if the measurement endpoint is a production of offsprings; however, without a valid NOAEC for the most sensitive bird selected, the LOAEC at the lowest test level is used instead to calculate a quotient.

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Table IV.1 Chronic Risk Quotients for One Application of Topramezone compared to a Mallard Duck LOAEC of 100.

Site	App. Rate (lbs a.i./acre)	Food Items	Maximum EEC mg/kg diet (ppm)	LOAEC (ppm)	Chronic RQ (EEC/LOAEC)
Corn (grain, seed, popcorn, sweet corn)	0.022	Short grass[27]	5-6	100	0.06

Since the estimated residues are so much lower than the dietary concentration at which no mortality occurred and at which some reproductive effects occurred, risk from direct effects is unlikely to birds, including endangered bird species.

The LOAEC for mallards is in question because there were some small, but statistically significant (p-value of 0.006) growth effects to offspring at 100 ppm, the lowest test level which a NOAEC could not be established. There was also weight loss for female adults (p-value of 0.021) at this level. While the effects were statistically significant, they were relative minor (<10%), and since the peak exposure levels are so much lower than this level, environmental effects are expected to be minimal.

Mammals

To assess risk to mammals, the acute oral LD_{50} of >2000 mg/kg was used to estimate LD_{50} s for mammals of various sizes assumed to occur in treated areas and exposed to treated food items. The rat LD_{50} and rat reproductive NOAEL was converted to representative exposed mammals using the following formula:

$$\text{Adj LD50} = (\text{TW/AW})0.25$$

Where,

TW=Tested animal Weight, 350 g for laboratory rat

AW=Assessed animal Weight

Table IV-2 shows the adjusted mammal LD_{50} and NOAEL..

[27] Other food items are not included here because residues on short grass are higher than any other food item and if residues on short grass are unlikely to be a risk, lower residues on other items would be unlikely to be a risk.

Table IV.2 Adjusted LD_{50} and NOAEL for various mammal weights

Mammalian Class	Assessed Animal Weight	% body wgt consumed	Adjusted LD_{50} mg/kg bw	Adjusted NOAEL
	15	95	> 4396	440
Herbivores/	35	66	> 3557	356
insectivores	1000	15	> 1538	154
	15	21	> 4396	440
Grainvores	35	15	> 3557	356
	1000	3	> 1538	154

The residue on food items were converted to daily doses based on mammal body weight and ingestion rates, see Table IV-6.

Table IV.3 Daily equivalent doses based on mammal weight and application rate

Mammalian Class	Assessed Animal Weight	% body wgt consumed	Adjusted LD50 mg/kg bw	Adjusted NOAEL
	15	95	> 4396	440
Herbivores/	35	66	> 3557	356
insectivores	1000	15	> 1538	154
	15	21	> 4396	440
Grainvores	35	15	> 3557	356
	1000	3	> 1538	154

The equivalent dose for all mammal classes is significantly lower than the adjusted LD_{50} s and NOAEL indicating low potential for acute and chronic risk. However, thyroid tumors were observed in the rat studies. Other effects were on the eye, pancreas, and skeletal variations. These effects are associated with inhibition of 4-HPPD.

2. Non-target Aquatic Animals and Plants

In this assessment, for acute toxicity to fish, invertebrates and aquatic plants, Tier II simulation Models PRZM and EXAMS were used to estimate peak surface water concentrations. The peak concentrations are then divided by the 96-hr LC_{50} for fish, 48-hr EC_{50} for invertebrates and EC50 for aquatic plants. The estimated peak concentrations of topramezone in the five different corn scenarios were < 2 μgL^{-1} (ppb).

(A)

Aquatic Animals

Freshwater and Estuarine/Marine Animals

Peak EECs were estimated for five different corn scenarios (See the "Aquatic Exposure Modeling" section). The highest estimated peak concentrations of topramezone were for 2 applications [28] (each at 0.011 lb ai per acre), with the second application 7 days apart as per label recommendation. These higher concentrations correspond to the Florida sweet corn scenario (Palm Beach County) The highest peak EECs for topramezone are 1.94 μgL^{-1} for aerial and 1.85 μgL^{-1} for ground applications. These peak concentrations are much lower than the acute LC_{50} s or EC_{50} s for freshwater and estuarine/marine animals greater than ~94 - 124 mg ai L^{-1} for most species, and mysid shrimp which had an LC_{50} 2.7 mg ai L^{-1} . This indicates that risk of direct acute effects is unlikely to all freshwater and estuarine/marine animals, including endangered species (Table IV.7) .

Reproductive risk to fish cannot be assessed, however, sublethal (survival of juveniles and growth) risk to fish can be assessed using the fish early life stage NOAEC of 2.93 mgL^{-1}. For invertebrates, reproductive risk can be assessed using the life cycle NOAEC of 48.6 mgL^{-1}. The highest EECs are significantly lower than this value suggesting low potential for sublethal chronic risk for fish and reproductive risk for invertebrates (Table IV.7).

Table IV.7 Acute and Reproductive Risks to Fish and Aquatic Invertebrates

Aquatic RQs based on Florida sweet corn scenario		
Assessed Organism	Acute RQ (peak EEC=1.94 $\mu g\ L^{-1}$)	Chronic (21-day EEC 1.91; 60-day EEC 1.9 $\mu g\ L^{-1}$)
Fish LC50 >94.6 mgL^{-1} NOAEC = 2.93 mgL^{-1}	<0.05	<1
Invertebrate (shrimp) EC50=2.7 mgL^{-1} Daphnid NOAEC = 48.6 mgL^{-1}	<0.05	<1

[28] Estimates of environmental concentrations in surface water were made for aerial and ground applications. Two applications regimes were modeled for each method of application. The application regimes are a single application at the maximum application rate of 0.022 lb ai/acre and for 2 applications each at 0.011 lb ai/acre and 7 days apart. Source: Proposed label for the end-use product.

The risk quotients for acute and sublethal risk to fish are lower than the LOCs indicating low potential for risk to aquatic vertebrates. The risk quotients for aquatic invertebrates, represented in this case by the most sensitive invertebrate, shrimp are lower than the LOC, indicating low potential for acute risk. The risk quotient for reproductive risk to invertebrate are lower than the LOC indicating minimal reproductive risk to invertebrates.

Further evaluation of the acute toxicity data for *Americamysis bahia* show that the data sets for the shrimp result in a dose response slope of 4.51 (95% C.I.: 2.59 - 6.42). Based on an assumption of a probit dose response relationship with a mean estimated slope of 4.51, the corresponding estimated chance of individual mortality/immobilization associated with the listed species LOC (0.05) of the acute toxic endpoint for estuarine/marine invertebrates is 1 in 4.51E+08. It is recognized that extrapolation of very low probability events is associated with considerable uncertainty in the resulting estimates. In order to explore the possible bounds to such estimates, the upper and lower values for the mean slope estimate (95% C.I.: 2.59 - 6.42) were used to calculate upper and lower estimates of the effects probability associated with the listed species LOC. The respective lower and upper effects probability estimates are 1 in 2660 and 1 in 1.00E+16. Although the acute toxicity data for freshwater invertebrates statistically supports the assumption of a probit dose response relationship, the confidence in estimated event probabilities for this taxonomic group is reduced by the large confidence intervals associated with the slope.

Aquatic Plants

Table IV.8 presents the RQs estimated from PRZM and EXAMS concentrations and vascular and nonvascular plant toxicity endpoints.

Table IV.8 Risk Quotients for Vascular and Non-vascular Plants for the use of Topramezone used on corn at a total maximum application rate of 0.022 lb ai/acre and applied in 2 single applications at 0.011 lb ai/acre and a re-application interval of 7 days and for a single application at 0.022 lb ai/acre.The maximum application rate per season is 0.022 lb ai/acre (25 g/ha). The EECs are the peak concentration for the five corn scenarios used in PRZM-EXAMS simulations

Scenarios	Taxa	No of Appls.	EEC (µg L⁻¹)	Toxicity (µg L⁻¹)		RQ	
			Peak	EC_{50}	NOAEC	Acute[2]	Endangered Species[3]
Corn, aerial Florida	Vascular (*Lemna gibba*)	2	1.94	8	1	0.24	**1.94***
		1	1.79	8	1	0.22	**1.79***
	Non-Vascular (*Pseudokirchneriella subcapitata*)	2	1.94	17000	3000	<0.01	<0.01
		1	1.79	17000	3000	<0.01	<0.01
Corn, ground Florida	Vascular (*Lemna gibba*)	2	1.85	8	1	0.23	**1.85***
		1	1.69	8	1	0.21	**1.69***
	Non-Vascular (*Pseudokirchneriella subcapitata*)	2	1.85	17000	3000	<0.01	<0.01
		1	1.69	17000	3000	<0.01	<0.01
Corn, aerial Illinois	Vascular (*Lemna gibba*)	2	1.32	8	1	0.17	**1.32***
		1	1.17	8	1	0.15	**1.17***
	Non-Vascular (*Pseudokirchneriella subcapitata*)	2	1.32	17000	3000	<0.01	<0.01
		1	1.17	17000	3000	<0.01	<0.01
Corn, ground Illinois	Vascular (*Lemna gibba*)	2	1.15	8	1	0.14	**1.15***
		1	0.99	8	1	0.12	0.99
	Non-Vascular (*Pseudokirchneriella subcapitata*)	2	1.15	17000	3000	<0.01	<0.01
		1	0.99	17000	3000	<0.01	<0.01
Corn, aerial Mississippi	Vascular (*Lemna gibba*)	2	1.46	8	1	0.18	**1.46***
		1	1.49	8	1	0.19	**1.49***
	Non-Vascular (*Pseudokirchneriella subcapitata*)	2	1.46	17000	3000	<0.01	<0.01
		1	1.49	17000	3000	<0.01	<0.01
Corn, ground Mississippi	Vascular (*Lemna gibba*)	2	1.31	8	1	0.16	**1.31***
		1	1.34	8	1	0.17	**1.34***

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Scenarios	Taxa	No of Appls.	EEC (μg L⁻¹)	Toxicity (μg L⁻¹)		RQ	
	Non-Vascular (*Pseudokirchneriella subcapitata*)	2	1.31	17000	3000	<0.01	<0.01
		1	1.34	17000	3000	<0.01	<0.01
Corn, aerial N. Carolina, East	Vascular (*Lemna gibba*)	2	0.82	8	1	0.1	0.82
		1	0.78	8	1	0.1	0.78
	Non-Vascular (*Pseudokirchneriella subcapitata*)	2	0.82	17000	3000	<0.01	<0.01
		1	0.78	17000	3000	<0.01	<0.01
Corn, ground N. Carolina, East	Vascular (*Lemna gibba*)	2	0.64	8	1	0.08	0.64
		1	0.58	8	1	0.07	0.58
	Non-Vascular (*Pseudokirchneriella subcapitata*)	2	0.64	17000	3000	<0.01	<0.01
		1	0.58	17000	3000	<0.01	<0.01
Corn, aerial Texas	Vascular (*Lemna gibba*)	2	1.37	8	1	0.17	1.37*
		1	1.34	8	1	0.17	1.34*
	Non-Vascular (*Pseudokirchneriella subcapitata*)	2	1.37	17000	3000	<0.01	<0.01
		1	1.34	17000	3000	<0.01	<0.01
Corn, ground Texas	Vascular (*Lemna gibba*)	2	1.24	8	1	0.16	1.24*
		1	1.2	8	1	0.15	1.2*
	Non-Vascular (*Pseudokirchneriella subcapitata*)	2	1.24	17000	3000	<0.01	<0.01
		1	1.2	17000	3000	<0.01	<0.01

1 The EC50 is used for the RQ for nonendangered species, the NOAEC is used for the endangered species

2 LOC >1 for risk to non-endangered species

* LOC >1 for risk to endangered species.

The most sensitive acute toxicity endpoint for vascular plants was frond number reduction. For non-vascular plants it was reduction in biomass.

Based on toxicity tests with vascular plants, parent topramezone (EC_{50} = 8.0 μgL⁻¹) was more toxic than the metabolite "M670H05" (EC_{50} = 360 μgL⁻¹) or the formulated topramezone (EC_{50} = 29.6 μgL⁻¹) used in the study.

According to the RQs, endangered vascular aquatic plants are at risk at levels of concern to the

Agency (i.e., RQs > 1.0) with the exception of a single ground application in Illinois and application(s) of ground or aerial in North Carolina (East). Although these estimates are only for a limited number of scenarios in potential use areas, there are exceedances resulting from multiple scenarios across the country, which suggests that risk is not limited to a small geographic location and that risk may be underestimated for some locations, but overestimated for others.

The Table also shows drift not to be a significant contributor to risk. Note that the RQs for aerial application are only slightly higher than those for ground application, indicating the primary route of exposure is runoff.

3. Non-target Terrestrial Plants in Dry-land and Semi-aquatic Habitats

Risks to terrestrial plants are based on RQs derived from the TERRPLANT model which estimates exposure from drift and runoff, both to dryland areas immediately adjacent to treated sites and to semi-aquatic areas receiving channelized runoff from treated areas. Non-endangered species risk quotients are presented in Tables IV.9 (aerial applications) and IV.10 (ground applications), and endangered species risk quotients are presented in Tables IV.11 (aerial applications) and IV.12 (ground applications).

Table IV.9. Topramezine EECs and **Nonendangered** Species Risk Quotients for Terrestrial Plants (0 022 bs ai./A; **Aerial** Application)
The EC25 is used to derive RQs for nonendangered plants

Crop Most Sensitive	Spray Drift (5%)		Spray Drift(5%) + Runoff to Dry and Wet Areas		
	Vegetative Vigor EC_{25}[1] (lbs ai/A)	EEC Risk Quotients Nonendangered Species	Seedling Emergence EC_{25}[2] (lbs ai/A)	EEC lb ai/acre Risk Quotients Nonendangered Species in Dry Areas	EEC lb ai/acre Risk Quotients Nonendangered Species in Wet Areas
Monocot	0.0098 dry weight onion	0.0011 lb ai/acre <1 RQ	0.042 dry weight ryegrass	0.0018 lb ai/acre <1 RQ	0.0077 lb ai/acre <1 RQ
Dicot	0.0001 dry weight soybean	0.0011 lb ai/acre **11 RQ**	0.0039 dry weight cabbage	0.0018 lb ai/acre <1 RQ	0.0077 lb ai/acre **1.9 RQ**

1. Vegetative vigor results are compared to spray drift because drift is simulated by the route of exposure in the vegetative vigor test.
2. Seedling emergent results are compared to exposure from runoff because exposure in the seedling emergent test simulates exposure in soil as occurs from runoff.

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Table IV.10. Topramezone EECs and **Non-endangered** Species Risk Quotients for Terrestrial Plants (0.022 bs ai./A; **Ground Application**) The EC25 is used to derive RQs for nonendangered plants.					
Crop Most Sensitive	Spray Drift (1%)		Spray Drift(1%) + Runoff to Dry and Wet Areas		
	Vegetative Vigor EC_{25}[1] (lbs ai/A)	EEC lb ai/acre Risk Quotients Non-Endangered Species	Seedling Emergence EC_{25}/NOAEC[2] (lbs ai/A)	EEC Risk Quotients Non-Endangered Species in Dry Areas	EEC Risk Quotients Non-Endangered Species in Wet Areas
Monocot	0.0098 dry weight onion	0.0002 lb ai/acre <1 RQ	0.043 dry weight ryegrass	0.0013 lb ai/acre <1 RQ	**0.0112 lb ai/acre** **<1 RQ**
Dicot	0.0001 dry weight soybean	0.0002 lb ai/acre <1 RQ	0.0039 dry weight cabbage	0.0013 lb ai/acre <1 RQ	**0.01122 lb ai/acre** **2.8 RQ**

1. Vegetative vigor results are compared to spray drift because drift is simulated by the route of exposure in the vegetative vigor test.

2. Seedling emergent results are compared to exposure from runoff because exposure in the seedling emergent test simulates exposure in soil as occurs from runoff.

Table IV.11. Topramezone EECs and **Endangered** Species Risk Quotients for Terrestrial Plants (0.022 bs ai./A; **Aerial** Application) The NOAEC is used to derive RQs for endangered plant species					
Crop Most Sensitive	Spray Drift (5%)		Spray Drift(5%) + Runoff to Dry and Wet Areas		
	Vegetative Vigor NOAEC[1] (lbs ai/A)	EEC lb ai/acre Risk Quotients Endangered Species	Seedling Emergence NOAEC[2] (lbs ai/A)	EEC lb ai/acre Risk Quotients Endangered Species in Dry Areas	EEC lb ai/acre Risk Quotients Endangered Species in Wet Areas
Monocot	0.005 dry weight onion	0.0011 lb ai/acre <1 RQ	0.015 dry weight ryegrass	0.0018 lb ai/acre <1 RQ	0.0077 lb ai/acre <1 RQ
Dicot	0.000009 dry weight soybean	0.0011 lb ai/acre **122 RQ**	0.0017 dry weight cabbage	0.0018 lb ai/acre **1 RQ**	0.0077 lb ai/acre **4.5 RQ**

1 Vegetative vigor results are compared to spray drift because drift is simulated by the route of exposure in the vegetative vigor test.

2 Seedling emergent results are compared to exposure from runoff because exposure in the seedling emergent test simulates exposure in soil as occurs from runoff.

Table IV.12. Topramezone EECs and Endangered Species Risk Quotients for Terrestrial Plants (0.022 bs ai./A; Ground Application) The NOAEC is used to derive RQs for endangered plant species					
Crop Most Sensitive	Spray Drift (1%)		Spray Drift(1%) + Runoff to Dry and Wet Areas		
	Vegetative Vigor NOAEC[1] (lbs ai/A)	EEC lb ai/acre Risk Quotients Typical2/Endangered Species	Seedling Emergence /NOAEC[2] (lbs ai/A)	EEC lb ai/acre Risk Quotients Endangered Species in Dry Areas	EEC lb ai/acre Risk Quotients Endangered Species in Wet Areas
Monocot	0.005 dry weight onion	0.0002 lb ai/acre <1 RQ	0.015 dry weight ryegrass	0.0013 lb ai/acre <1 RQ	0.0112 lb ai/acre <1 RQ
Dicot	0.000009 dry weight soybean	0.0002 lb ai/acre **24 RQ**	0.0017 dry weight cabbage	0.0013 lb ai/acre <1 RQ	0.0112 lb ai/acre **6.6 RQ**
1. Vegetative vigor results are compared to spray drift because drift is simulated by the route of exposure in the vegetative vigor test. 2. Seedling emergent results are compared to exposure from runoff because exposure in the seedling emergent test simulates exposure in soil as occurs from runoff.					

Spray Drift Risk to Terrestrial Plants

The AgDRIFT Tier I model for ground and aerial application was used to estimate how far from the treated field non-target plants would be affected in an effort to provide information on the feasibility of using spray drift buffers to protect plants. Appendix E contains a bar graph that shows the percent effects for tested species at a range of distances down wind up to 1000 feet. It shows that for corn, rye grass and wheat there would not even be a 10% effect, immediately adjacent to the treated field. Conversely, beans and lettuce would be affected at the 25% level up to about 100 feet. Buffers of 100 feet would protect plants from effects of 25% that have sensitivities similar to beans and lettuce. However, radish, tomato and cabbage are more sensitive, and would experience 25% effects at 200 to 300 feet. Species that have sensitivity similar to soybean, the most sensitive species tested, are expected to experience up to 25% effects up to, and over 1000 ft.

B. Risk Description - Interpretation of Direct Effects

1. Risks to Terrestrial and Aquatic Plants

The results of this risk assessment suggest the potential for direct effects to both non-endangered and endangered terrestrial plants, and endangered aquatic vascular plants.

Specifically, RQs for the following receptors exceed risk levels of concern established for the Agency for the screening-level risk assessment:

Terrestrial plants: RQs exceed non-endangered and endangered dicot LOCs. (RQ ranges from 1.04 to 122; Agency's Level of Concern is 1); RQs do not exceed non-endangered and endangered monocots LOCs

Aquatic plants: RQs exceed endangered vascular species LOCs (RQ = 1.9; Agency's Level of Concern is 1. RQs do not exceed non-endangered vascular, non-endangered and endangered nonvascular species LOCs.

Terrestrial Plants

Terrestrial plants actively growing in dry or wet areas adjacent to agricultural fields may be at risk as a result of runoff and/or drift. In addition to considering where plants grow, exposure must be estimated to compare with results from two kinds of plant tests - a seedling emergence study and a vegetative vigor study. The seedling emergence study involves treating the soil in which seedlings grow, thus, exposing the growing plant to the pesticide. The vegetative vigor study involves exposing only the foliage of actively growing plants off-site to spray drift Both spray drift and runoff are assumed to reach off-site soil. The risks to emerging seedlings and 2-4 true leaf stage plants are discussed in greater detail below.

Emerging seedlings in dry areas receiving sheet runoff (1:1 ratio) from adjacent treated areas:

- Potential risk from a combination of runoff and drift to non-endangered emerging seedlings (based on seedling emergence EC_{25}) is not expected when applying by air or ground (RQ ranges from 0.03 to 0.45; Agency's Level of Concern is 1).

- Potential risk from a combination of runoff and drift to endangered emerging seedlings (based on seedling emergence NOAEC) may be expected when applying by air (RQ = 1.0; Agency's Level of Concern is 1), but not expected for ground application.

Emerging seedling in wetlands or areas receiving channelized runoff (10:1 ratio) from adjacent treated areas:

- Potential risk from a combination of runoff and drift to non-endangered and endangered emerging seedlings (based on both seedling emergence EC25 and NOAEC) may be expected when applying by air (RQ ranges from 1.9 to 4.5) or ground (RQ ranges from 2.9 to 6.6; Agency's Level of Concern is 1).

  Plants approaching the 2-4 true leaf stage in adjacent areas receiving 5% and 1% drift alone from aerial and ground application, respectively, in treated areas:

- Potential risk from drift to non-endangered plants (based on vegetative Vigor EC25) may be expected for aerial application (RQ = 1.1; Agency's Level of Concern is 1), but not expected for ground application.
- Potential risk from drift to endangered plants (based on vegetative vigor NOAEC) may be expected when applying by (RQ = 122) air or ground (RQ = 24; Agency's Level of Concern is 1).

The tested terrestrial plants exhibited a wide range of sensitivity to topramezone (see Appendix E, Figure 1). Seedling emergence EC_{25} values ranged from >0.045 (soybean and monocots, dry weight) to 0.0039 lbs ai/A (cabbage, dry weight), while seedling emergence $NOAEC/EC_{05}$ values.

ranged from 0.045 (soybean and monocots, dry weight) to 0.002 lbs ai/A (cabbage, dry weight). If applied at the proposed labeled rate of 0.022 lb ai/A, 5 out of 10 tested species in the emergence study may be affected when exposed to topramezone.

The seedling emergence and vegetative vigor studies suggest this chemical exhibits considerable toxic selectivity. It can be assumed that there may also be similar variation in the general non-target plant population. However, there are uncertainties in having ten tested species represent the universe of non-target plant species. In addition, measurable endpoints were based on growth effects (shoot weight, shoot height) and observed physical injury. Currently, EPA does not measure reproduction effects in plants and therefore is not able to adeptly characterize herbicidal effects such as chlorosis (discoloration) and necrosis.

Further evaluation of the observed injuries to plants from topramezone reveals at an observed application rate of 0.015 lb ai/A, chlorosis and necrosis is most pronounced for those crops: soybean, lettuce, radish, tomato and cabbage. This should be taken in consideration in terms of crop rotation or one of the above crop is found on adjacent agricultural sites. For example, if soybeans follow corn on a field where topramezone is applied to corn, then effects to soybeans, which are sensitive to topramezone, could be observed.

Aquatic Plants

Aquatic plants actively growing in static water bodies adjacent to agricultural fields may be at risk as a result of a combination of runoff and/or drift. In addition to considering where plants grow, exposure must be estimated to compare with results from two kinds of plant tests - an aquatic vascular study and an aquatic nonvascular study. The risks to vascular and nonvascular plants are discussed in details below.

Vascular plants in water bodies receiving runoff and drift from adjacent treated areas:

- Potential risk from a combination of runoff and drift to non-endángered vascular plants (based on duckweed EC_{50}) is not expected for aerial or ground application.

- Potential risk from a combination of runoff and drift to endangered vascular plants (based on duckweed NOAEC) may be expected for aerial (RQ = 1.9) and ground application (RQ = 1.6; Agency's Level of Concern is 1) with the exception of ground application in Illinois and application(s) of ground or aerial in North Carolina (East)

Nonvascular plants in water bodies receiving runoff and drift from adjacent treated areas:

- Potential risk from a combination of runoff and drift to non-endangered and endangered nonvascular plants (based on *Pseudokirchneriella subcapitata* EC_{50} and NOAEC) are not expected for aerial or ground application.

Direct Effects to Plants Related to the Mode of Action of Topramezone

This analysis of direct effects on plants is based on the mode of action of topramezone. Topramezone, like isoxaflutole[29] and mesotrione, inhibits the HPPD enzyme (4-hydroxyphenyl-pyruvate-dioxygenase,4-HPPD)[30], which is involved in regulating the biosynthesis of carotenoids. Inhibition of carotenoid biosynthesis causes "bleaching" in plants. Topramezone is absorbed by

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[29] There are incidents reported for isoxaflutole related to discoloration of corn, even though corn is the target crop.

[30] See http://www.plantprotection.org/HRAC/MOA.html
The HPPD enzyme is also present in animals and it is a tyrosine regulator

the leaves, roots and shoots, then translocated to the growing points of the sensitive weeds. This causes a strong bleaching activity on the growing zones of the shoots within 2-5 days ofapplication. Exposure to light causes necrosis of chlorotic tissues and eventual plant death within 14 days after application . More detailed information on the mode of action of topramezone and other 4-HPPD inhibitors was presented under the "Mode of Action" section.

a. *Direct effects from off-target exposure (runoff and spray drift)*

Both terrestrial plant studies are limited to 21-day data and at the time when plants are at an early developmental stage (seedlings; and growing plants). None of the current guideline studies address the effects of a herbicide at higher stages of development, such as flowering, fruiting, and ripening (i.e., when pigmentation is likely to be more active) .

The terrestrial plant assessment was based on the most sensitive endpoint, in this case dry weight. However, other effects were observed that were significant and even detrimental. In vegetative vigor studies, tomato and radish, two species that are well known to be rich in carotenoids showed chlorosis and necrosis at a significant percent (> 90%). Dicots were identified as the most sensitive terrestrial plants and are more likely to be affected by topramezone than monocots.

Although the available plant data is very limited to go beyond an assessment at the screening level, the mode of action of topramezone (or other 4-HPPD inhibitors, such as isoxaflutole and mesotrione) raise the following issues:

1. The variability in time of enzyme development for different plants and if inhibition of 4-HPPD is such that the plant cannot recover and advance to higher developmental stage. That is, if different plants can or cannot recover from the chemical stress at early stages of development.

2. The variability in flowering, fruiting, and fruit pigmentation stages among plants, to what extent pigmentation is inhibited, and for how long. Therefore, there is a potential for direct effects to non-target plants at more advanced developmental stages. This is an issue that cannot be resolved from the current Tier II Plant Testing studies, which do not test plants at the pre-flowering, fruiting and other active pigmentation stages.

Examples of plants rich in carotenoids are tomato, radish (both used in the Tier II plant studies), most fruits such as pineapples, oranges, strawberries and others, and flowers like narcissus.

b. *Direct effects from inadvertent exposure to residues of topramezone*

Ground and/or surface water is used to not only irrigate crops (or commercial ornamental plants), but also plants in residential sites or public spaces. Residues of topramezone in irrigation water are a source of inadvertent exposure.

Risk Quotients for non-endangered and endangered plants were calculated from the estimated concentrations of irrigation water drawn from ground water and surface water and the most sensitive endpoints identified in the vegetative vigor studies. The estimated concentration in irrigation water from surface water is based on a maximum peak concentration of 1.94 μgL^{-1} (PRZM-EXAMS; Florida sweet corn scenario). The estimated concentration in irrigation water from ground water was based on 0.067 μgL^{-1}, as estimated by SCI-GROW. Assumptions and calculations to estimate inadvertent concentrations of topramezone in irrigation water are included in Appendix E.

Table IV.13 Risk Quotients for Non-endangered and Endangered Plants Irrigated with Ground and Surface Water Containing Residues of Topramezone [1]

Plant	Ground water	Surface water
Non-endangered Monocots.	1.52 x 10-4	0.044
Non-endangered Dicots	1.52 x 10-3	0.44
Endangered Monocots	0.003	0.09
Endangered Dicots	**1.69**	**49**

1 Estimated concentrations of topramezone in irrigation water:

1.52 x 10-6 μgL^{-1} (ground water) and 4.4 x 10-4 μgL^{-1} (surface water).

Vegetative vigor endpoints (dry weight),

Non-endangered: 1×10^{-2} (monocots;onions) and 1×10^{-3} (dicots; soybeans)

Endangered: 5×10^{-3} (monocots;onions) and 9×10^{-6} (dicots;soybeans)

Levels of Concern are exceeded for endangered plants irrigated with ground or surface water containing residues of topramezone..

b. *Direct effects from inadvertent exposure from soil dust containing residues of topramezone and/or potentially active metabolites*

Topramezone and its soil metabolite "M670H01" may bind to soils via hydrogen bonding to humic components of soil and/or via chelation to Fe(II) species on soil, even though topramezone is an anion and not expected to bind.. Soil and water-sediment studies have shown that non-extractable residues in soils/sediments increase with time and that time-dependent sorption appears to control the overall dissipation of topramezone. These residues (parent; metabolites) may remain intact and desorb slowly. That is, topramezone and/or metabolites may then become bioavailable. Therefore, topramezone and/or metabolites have the potential to be transported by soil dust deposited on off-target sites long after treatment. Desorption in the non-target fields may cause direct effects on emerging seedlings.

2. Risks to Terrestrial and Aquatic Animals

The results of the risk characterization with terrestrial and aquatic animals suggest that there are no acute and chronic risks associated with avian, mammal, fish, and invertebrate exposures to topramezone and its formulated product, as appropriate. The risks associated with all of the terrestrial and aquatic animals are discussed in greater detail below.

Birds and Mammals

As shown in Table IV.4, all avian acute and chronic Risk Quotients (RQs) are less than the Level of Concerns (LOCs). Therefore, the acute and chronic risks to birds and mammals are presumed to be negligible.

Further evaluation of the avian reproduction studies with the Northern bobwhite quail and Mallard duck shows an uncertainty in the toxicity results. The mallard duck appears to be more sensitive to topramezone than the bobwhite quail, however, a LOAEC value of 100 ppm ai for the mallard duck was obtained to characterize the reproductive risks to birds. Treatment-related effects seen in the bobwhite quail and mallard duck were reduction in the ratio of number hatched to live embryos at 1012 ppm ai and reduction in hatchling body weight and female weight gain at all three treatment levels, respectively. Although, the estimated environmental concentration (EEC) was estimated to be ~5 ppm which is approximately 20 times below the lowest concentration tested in the duck study. EFED is requesting the mallard duck study to be repeated to establish a NOAEC. If multiple applications or an increase in the application rate of topramezone is requested in the future, the avian reproductive test with the mallard duck will be of a greater value.

Precautionary Labeling for Terrestrial Invertebrates

Although EFED does not estimate risk quotients for terrestrial invertebrates, acute and subchronic toxicity studies to terrestrial invertebrates were completed for active ingredient topramezone (BAS 670H) and the formulated product (BAS 670 00H). No significant mortality and/or sublethal effects were observed in any of the treatment groups; therefore, terrestrial invertebrates exposures to topramezone and its formulated product in soil are not likely to be at risk. Precautionary labeling is not required for those terrestrial invertebrates as follows:

- honeybees
- earthworms
- carabid beetle
- lacewings
- predatory mites
- parasitoids

3. Incidents Involving Terrestrial and Aquatic Animals and Plants

No incident information is found in the Ecological Incident Information System (EIIS) database, since topramezone is petitioned for registration as a new chemical. In addition, there are no open literature data on topramezone that may indicate use related incident. However, there are incident involving plants for isoxaflutole and mesotrione, both of which share the same mode of action with topramezone.

4. Federally Threatened and Endangered (Listed) Species Concern

For listed species assessment purposes, the action area is considered to be the area affected directly or indirectly by the Federal action and not merely the immediate area involved in the action. At the initial screening-level assessment, broadly described taxonomic groups are considered and thus conservatively assumes that listed species within those broad groups are co-located with the pesticide treatment area. This means that terrestrial plants and wildlife are assumed to be located on or adjacent to the treated site, and aquatic plants and organisms are assumed to be located in a surface water body adjacent to the treated site. The assessment alsoassumes that the listed species are located within an assumed area which has the relatively highest potential exposure to the pesticide, and that exposures are likely to decrease with distance from the treatment area.

In Section II.A.4 of this screening-level assessment for topramezone presents the pesticide use sites that are used to establish initial collocation of species with treatment areas. If the assumption associated with the screening-level action area result in RQs that are below the listed species LOCs, a "no effect" determination conclusion is made with respect to listed species in that taxa, and no further description of an action area is necessary. Furthermore, RQs below the listed species LOCs for a given taxonomic group indicate no concern for indirect effects upon listed species that depend upon the taxonomic group covered by the RQ as a resource.

However, in situations where the screening assumptions lead to RQs in excess of the listed species LOCs for a given taxonomic group, a potential for a "may effect" conclusion exists and may be associated with direct effects on listed species belonging to that taxonomic group or may extend to indirect effects upon listed species that depend upon that taxonomic group as a resource. In such cases, additional information on the biology of listed species, the locations of these species, fate and transport properties of the chemical, and the locations of use sites could be considered to determine the extent to which screening assumptions regarding an action area apply to a particular listed organism. These subsequent refinement steps could consider how this information would impact the action area for a particular listed organisms and may potentially include areas of exposure that are downwind and downstream of the pesticide use site.

5. Data Related to Under-represented Taxa

Ecotoxicity studies are conducted with a very limited number of species as surrogates for members of the same species. Moreover, neither reptiles or amphibians are test organisms. Risk characterization for reptiles relies on data from birds, which is also based of a very limited number of bird species. Likewise, risk characterization for amphibians uses fish data conducted in a very limited number of fish species. Acute toxicity studies conducted with rats or mice are extrapolated to represent acute toxicity to all mammals (including aquatic mammals), whereas 2-generation studies with rats are used to assess reproductive effects on mammals.

Based on these extrapolations, topramezone does not pose risk to animals if used on corn and accordingly to the proposed label.

Plant studies (seedling emergence and vegetative vigor) for topramezone were limited to 10 plants to represent all monocots and all dicots. Moreover, all of the plants used in these studies are commercial crops. For the aquatic risk assessment, one surrogate species was used to represent all aquatic vascular plant and four surrogate species were used to represent all non-vascular plants. In addition, plant studies are not designed to provide data at developmental stages beyond those required by the guideline.

6. Implications of Sub-lethal Effects

a. Indirect Effects Analysis

Potential direct effects of topramezone based on its mode of action were previously discussed Pigmentation inhibition to non-target plants was identified as a potential direct effect. Potential indirect effects that may be associated with the mode of action of topramezone are:

1. Plants "depleted" of carotenoids not only loose in esthetic appearance, but also in nutritional value. Consider, for example, β-carotene as a precursorto Vitamin A.

2. Many insects (or other animals) are attracted to flowers or fruits by their color. Discoloration of petals by inhibition of carotenoid biosynthesis may result in food source loss for the animals.

Other potential indirect effects could be:

1. Aquatic organisms may be indirectly affected due to loss of cover or food sources.

2. Structural changes in the aquatic plant communities due to variable species sensitivity and resistance. This could result in changes further up the aquatic food chain.

b. Critical habitat

In the evaluation of pesticide effects on designated critical habitat, consideration is given to the physical and biological features (constituent elements) of a critical habitat identified by the U.S Fish and Wildlife and National Marine Fisheries Services as essential to the conservation of a listed species and which may require special management considerations or protection. The evaluation of impacts for a screening level pesticide risk assessment focuses on the biological features that are constituent elements and is accomplished using the screening-level taxonomic analysis (risk quotients, RQs) and listed species levels of concern (LOCs) that are used to evaluate direct and indirect effects to listed organisms.

The screening-level risk assessment has identified potential concerns for indirect effects on listed species for those organisms dependent upon terrestrial and aquatic plants. In light of the potential for indirect effects, the next step for EPA and the Service(s) is to identify which listed species and critical habitat are potentially implicated. Analytically, the identification of such species and critical habitat can occur in either of two ways. First, the agencies could determine whether the action area overlaps critical habitat or the occupied range of any listed species. If so, EPA would examine whether the pesticide's potential impacts on non-endangered species would affect the listed species indirectly or directly affect a constituent element of the critical habitat. Alternatively, the agencies could determine which listed species depend on biological resources, or have constituent elements that fall into, the taxa that may be directly or indirectly impacted by the pesticide. Then EPA would determine whether use of the pesticide overlaps the critical habitat or the occupied range of those listed species. At present, the information reviewed by EPA does not permit use of either analytical approach to make a definitive identification of species that are potentially impacted indirectly or critical habitats that is potentially impacted directly by the use of the pesticide. EPA and the Service(s) are working together to conduct the necessary analysis.

This screening-level risk assessment for critical habitat provides a listing of potential biological features that, if they are constituent elements of one or more critical habitats, would be of potential concern. These correspond to the taxa identified above as being of potential concern for indirect effects and include the following terrestrial and aquatic plants. This list should serve as an initial step in problem formulation for further assessment of critical habitat impacts outlined above, should additional work be necessary.

c. Co-occurrence Analysis

EFED used the LOCATES[31] database to identify listed species located in counties known to produce corn, the crop upon which the pesticide will be used. This screening level assessment considers both direct and indirect effects across generic taxonomic groupings; therefore, plants and species that may depend on plants for the assessment endpoints considered in this assessment were identified. Plant species were further divided into monocots and dicots. **Although LOCs were not exceeded for any monocot plant tested, topramezone is a herbicide for post-**

[31] LOCATES is a Lotus Approach database used in EFED to identify threatened and endangered (T&E) species that may be adversely affected by use of toxic pesticides on a specified crop or crops. The database identifies counties where T&E species may occur and where the acreage grown of a crop or crops exceeds a specified threshold level (e.g., >10 acres).

emergence control of grasses. Therefore, there are potential adverse effects to some monocots because topramezone is proposed as a herbicide to control emerged grasses in corn fields. Further habitat analysis is needed to allow for a determination of potential risk to listed dicot plants. Monocot and dicot species located in corn-growing counties of the United States are in Appendix H and are summarized in Table IV.14.

TableIV.14. Number of Monocots and Dicots Located in Corn-Growing Counties

Crop	Number of Monocotsa	Number of Dicots and Other Plantsa
Field Corn	32	262
Sweet Corn	52	385
Pop corn	6	20
Grain and Seed	22	185

a Although adverse effects may not be expected for the tested monocots, topramezone can be used to control post-emergent grasses. Therefore, there is potential risk for some monocots. Further analysis is needed to determine potential risk to dicots and other plants.

d. Indirect Effects Co-Occurrence Analysis

LOCATES was also used to identify listed species that depend on plants for survival, fecundity,or reproduction that reside in corn-growing counties in the United States. Because plants are primary producers, all taxonomic groups included in LOCATES were included in this analysis (mammals, birds, insects, fish, aquatic invertebrates, arachnids, snails, reptiles, and amphibians). For these taxonomic groups, EFED performed a preliminary analysis to identify species that are unlikely to be indirectly affected by potential effects on dicots from topramezone uses. These species, and basis for the designation, are in Appendix H and are summarized in Table IV.15, below.

Table IV.14. Number of Species Identified that are Unlikely to be Indirectly Affected by Potential Direct Effects to Dicots and Number of Species Identified Where Further Evaluation is Needed (All Proposed Uses)			
Animal	**No. of Species Identified as Unlikely Affected**	**No. of Species Where Further Analysis is Needed**	**Comment**
Mammals	27	32	Habitat, home-range, and diet were used for preliminary analysis. Carnivores with large home ranges or species whose habitats and diets were inconsistent with agriculture were identified as unlikely adversely affected
Birds	20	35	Habitat, home-range, and diet were used for preliminary analysis. Carnivores with large home ranges or species whose habitats and diets were inconsistent with agriculture were identified as unlikely adversely affected
Fish	77	29	Fish species were subdivided by diet. Species that do not consume plants were identified as unlikely indirectly affected by topramezone.
Arachnids	20	0	All arachnids were either obligate subterraneous species or are located in high-elevation forests.
Amphibians	0	18	Preliminary analysis has not been conducted.
Aquatic Invertebrates	0	89	Preliminary analysis has not been conducted.
Insects	0	39	Preliminary analysis has not been conducted.
Reptiles	0	28	Preliminary analysis has not been conducted.

C. Description of Assumptions, Limitations, Uncertainties, Strength, and Data Gaps

a. Assumptions, Limitations. Uncertainties. Strength. and Data Gaps Environmental Fate Data and Exposure Assessment.

In the "Problem Formulation" chapter, several sources of uncertainty in the environmental fate data were identified. Considering that the data is used to select input parameters for aquatic exposure assessment, these uncertainties are carried into the exposure assessment. These environmental fate uncertainties are discussed in more detail in this chapter.

As a new chemical for which the use areas are not known, generic, rather than region specific assessments can only be performed at the screening level. In addition, corn is widely cultivated in the USA and corn is grown in a wide variety of soils, climates, ecosystems, and agricultural practices. Therefore, risk may be underestimated for some geographical regions and underestimated for others.

Most of the environmental fate studies were well conducted and provided reliable data for characterizing the environmental fate of topramezone and estimating environmental concentrations. However, deficiencies were identified in some of the studies that can introduce uncertainty in the assessment and EECs. Topramezone is stable in abiotic media (hydrolysis; direct photolysis) and even towards indirect photolysis. Although biotransformation was identified as a route of dissipation, further assessment and integration of data indicate that kinetically controlled adsorption to soil/sediments (i.e, time-dependent sorption) may be competing with biotransformation as a dissipation route. Specific identified issues are presented below.

1. Effect of pH in exposure and toxicity of topramezone

Topramezone is a weak acid, with a pK_a of 4.06 and, therefore the concentration of the dissociated form increases with pH and, in principle, its mobility in soils is expected to increase, provided that other binding mechanisms (e.g., chemisorption or hydrogen bonding) do not control sorption behavior of topramezone. Given the very narrow pH range of the soils used in the batch-equilibrium adsorption/desorption studies could not be established. Assuming that sorption behavior correlates with pH and given the extensive variability in soils across the potential use area of topramezone, exposure concentrations of topramezone in aquatic environments may be underestimated or overestimated for specific sites.

2. Time-dependent sorption behavior

Batch-equilibrium adsorption/desorption are short term studies (24 hr or, at the most 48) and are not designed to study the kinetics of sorption. That is, how fast the chemical absorbs and how fast it desorbs (time-dependent adsorption and desorption). In all of the soil and water-sediment systems, non-extractable radioactivity increased with time and was predominantly associated with the fulvic acid fraction. It is conceivable that biotransformation and adsorption are competitive processes and that the observed dissipation of topramezone may be controlled by adsorption rather than by biotransformation.

Topramezone can be envisioned as a chelating ligand and it is chelation to the Fe(II) site of the 4-HPPD enzyme what makes topramezone a 4-HPPD inhibitor. The structural requirements for herbicides that inhibit the functions of 4-HPPD were discussed under the mode of action of topramezone. In the same manner that the keto (carbonyl) and the enolate can bind to the Fe (II) site of the enzyme, it can be speculated that there are two possible ways by which topramezone could bind to soil. One way is via hydrogen bonding to terminal hydroxyl (-OH) and/or carbonyl (keto) groups in organic matter (e.g., humic and fulvic acids in soil and/or present on the surfaces of clays). Another way is by chelation to Fe surface sites of iron mineral phases (crystalline and/or amorphous) that may be present in soils and sediments. Chelation to other metal sites such as Mn and Cu cannot be ruled out. Time-dependent sorption of topramezone may be related to changes it the conformation of the molecule over time that can optimize hydrogen bonding and/or chelation. Factors that may contribute to desorption are those that could weaken hydrogen bonding and/or chelation to metal sites, for example, changes in ionic strength of the media.[32]

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32 J. Buffle. **Complexation Reactions in Aquatic Systems: an analytical approach**. Published by Ellis Horwood, New York., 1990.
W. Stumm. **Chemistry of the Solid-Water Interface: Processes at the Mineral-Water and Particle-Water Interface in Natural Systems**. Published by Wiley Interscience, New York., 1992
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A. Cotton and G. Wilkinson. **Advanced Inorganic Chemistry**. Fifth Edition. Published by John Wiley and Sons, New York, 1988.
N.N. Greenwood and A. Earnshaw. Chemistry of the Elements. Published by Pergamon Press, New York, 1984.

3. Behavior of topramezone in water-sediment systems

Although the study has deficiencies that must be addressed by the registrant, a marked difference was found between the types of metabolites formed in water-sediment systems under aerobic and anaerobic incubation.

Metabolite formation

The soil metabolite "M670H05" was not found in the water-sediment studies., although this metabolite could only enter surface water by runoff or via eroded soil. Although there are animal toxicity data for this metabolite, no plant data are available). Therefore, the toxicity of this metabolite to aquatic plants is not known. However, the limited number of water- sediment systems used in the studies does not preclude that M670H05 could also form in some water - sediment systems.

The metabolite "M670H01" (the "cyano" metabolite, this metabolite is a "ketonitrile) was found in one aerobic soil and in the aerobic water-sediment system. No transformation of the cyano group to an amide and to a carboxylic acid group was found in the study, but such pathway is feasible (it is well documented for cyanazine). There are no toxicity data for "M670H01", even though this metabolites have the molecular structure features required for a 4-HPPD inhibitor and it is very similar to an active metabolite of isoxaflutole (RPA-202248, also a "ketonitrile")..

The metabolite "M670H10" was the only one identified under anaerobic conditions. It is clear that reduction was involved in the formation of this metabolite, as the sulfonyl group, S(VI), of topramezone is reduced to a sulfide, (S-II), which is consistent with redox chemistry in anoxic environments.. There are no toxicity data for this metabolite. An EPIWIN estimate of physical and chemical properties of the metabolite indicate that this metabolite was the most hydrophobic of all of the metabolites (Log Kow = 2.75). The metabolite "M670H10" have higher adsorption coefficients than parent topramezone or "M670H05). In the batch-equilibrium adsorption/ desorption study conducted with this metabolite (46242703), the authors argue that the exposure to aquatic organisms would decrease by partitioning into the sediment. However, long term persistence in sediments (and potential accumulation) nor its time-dependent sorption is not well understood. There are no toxicity data for "M670H10", even though this metabolite also has the molecular structure features required for a 4-HPPD inhibitor.

Persistence

Marked differences in kinetics and transformation products were found between the two studied aerobic - water sediment system. In a river water -sediment system, topramezone was persistent throughout the 120 days duration of the study and no metabolites were identified. In a pond water-sediment, the total system half-life of topramezone was 19 days and the metabolite "M670H01" was identified. But major differences were found between the physical and chemical characteristics of the pond water-sediment and the river water-sediment systems:

i. The sediment in the pond water was acidic.
ii. The pond water had a high electrical conductivity and high "dissolved solids"

Thus, the following explanations are plausible: (a) Dissipation is related to microorganisms typical of an acid environment; (b) Ionic species may be involved; (c) Colloidal material may contribute to surface-catalyzed reactions; (d) "Disappearance" of topramezone is dominated by adsorption rather than by biotransformation, particularly if the colloidal material is significant, as colloids provide a much higher surface area (adsorption sites) than larger particulates.

Although the design of the guideline study is not geared to identify such contributions, the pond water-sediment system is nevertheless atypical of ponds that may be found in sites where topramezone might be used. Therefore, how persistent topramezone is in aerobic water-sediment systems is not well understood. Because aerobic soil half-life is an important input parameter in aquatic exposure models, this uncertainty is carried over to the estimated exposure concentrations, as assumptions had to be made (in this case the 2 x aerobic soil metabolism recommended default value). Therefore, exposure concentrations may have been underestimated or overestimated as a result of this uncertainty.

The Agency has requested that the petitioner addresses the identified deficiencies. This information is important to better define the behavior of topramezone in aquatic environments.

Soils

The potential for carryover of the aerobic soil metabolite M670H05 (which appears to form only in aerobic soils) was identified, but it could not be adequately assessed because no aerobic soil metabolism data were available beyond 1 year post-application that would indicate that the amount of this metabolite keeps increasing. There are no seedling emergence data for this metabolite that could be used to evaluate its phytotoxicity to emerging, non-target plants.

Considerable variability in persistence of topramezone and nature and relative ratio of metabolites was observed in the six aerobic soils. Therefore, based on soil differences (including microbial activity) it is expected that the persistence of topramezone, nature and relative amount of metabolites will be highly variable across the potential use area.

Temperature at the time of application and throughout the growing season can control the persistence of a pesticide in the environment. The aerobic soil metabolism studies were conducted only at one temperature (27° C), and therefore, persistence at lower temperatures. Given the regional variability of corn agricultural practices, topramezone may persist longer when it is applied at temperatures lower than the study temperature. Topramezone may persist longer in colder, northen climates that in the south. As a result, exposure concentrations in surface water (or amount of residues in soil) may be overestimated or underestimated for specific areas.

In addition, carryover of topramezone from season-to-season can not be ruled out if adsorption to soils as "non-extractable" residues is taken into account. The extent of bioavailability via desorption is not known, as the batch-equilibrium adsorption/desorption studies are not designed to study the kinetics component of sorption. Thus, soils or sediments may act as reservoirs to store topramezone.

b. Assumptions, Limitations, Uncertainties, Strength, and Data Gaps in Characterization of the Effects Characterization and their Implications to the Ecological Risk Assessment.

Terrestrial

1.. The terrestrial assessment accounts only for exposure of terrestrial organisms to topramezone, but not to its metabolites. The potential toxicity of soil metabolites (M670H05 and M670H01) is unknown. The only toxicity data submitted is with M670H05, but was conducted only with aquatic organisms. The effect of these two metabolites on seedling emergence is not known. However, "M670H01" exhibit those molecular features associated with 4-HPPD inhibitors.

2. The risk assessment only considers the most sensitive species tested. Terrestrial acute and chronic risks are based on toxicity data for the most sensitive bird, mammal, and plant species tested. Responses to a toxicant can be expected to be variable across species. The position of the tested species relative to the distribution of all species' sensitivities to topramezone is unknown. This is of particular concern for topramezone effects on plant because this herbicide is selective and some plant species are likely to be more sensitive than others. In addition, plant studies are not conducted at the flowering, fruiting and fruit maturity stages. At these stages, plants may be more sensitive to topramezone because topramezone may affect pigment biosynthesis. There are no protocols for plant testing at higher developmental stages.

3.. The risk assessment only considered a subset of possible use scenarios. For this risk assessment, the scenarios represented only a limited number of potential use sites. As a new chemical, only potential use areas can be identified. A greater risk to the environment than those included in this risk assessment may be for those occurring in or near sensitive environments (e.g., close proximity to habitat that supports or has the potential to support endangered or threatened terrestrial species).

4.. Only dietary exposure is included in the exposure assessment. Other exposure routes are possible for animals in treated areas. These routes include ingestion of contaminated drinking water, ingestion of contaminated soils, preening/grooming, dermal contact, and inhalation. Consumption of drinking water would appear to be inconsequential if water concentrations were equivalent to the concentrations from PRZM/EXAMS; however, puddled water sources on treated fields may have much higher concentrations than those modeled ponds. Preening exposures, involving the oral ingestion of material from the feathers remains an non-quantified, but potentially important, exposure route considering that the mode of herbicide action of topramezone is inhibition of the HPPD enzyme. This enzyme is also present in mammals and controls tyrosine catabolism. Thyroid effects on wild mammals is not known, but were observed in tests conducted with rats.

5.. The risk assessment assumes 100% of the diet is relegated to single food types foraged only from treated fields. These assumptions are likely to be conservative for many species and will tend to overestimate potential risks. The assumption of 100% diet from a treated area may be realistic for acute exposures, but long-term exposures modeled as single food types composed entirely of material from a treated field is uncertain.

Aquatic

1. The risk assessment only considers the most sensitive species tested. Aquatic acute and chronic risks are based on toxicity data for the most sensitive fish, invertebrate, and plant species tested. Responses to a toxicant can be expected to be variable across species. Sensitivity differences between species can be considerable (several orders of magnitude) for some chemicals (Mayer and Ellersieck 1986). It is uncertain if the tested laboratory species is representative of most species' sensitivities to topramezone toxicity.

2. There are no toxicity data for the metabolites "M670H01" (which is also a soil metabolite) and "M670H10", which have been identified as forming in water-sediment systems and have molecular features that suggest potential behavior as 4-HPPD inhibitors.

3. Topramezone has a proposed label only for corn, which is grown over a large geographic area. For this risk assessment, the scenarios selected for PRZM-EXAMS simulations represented only a finite number of areas where this chemical might be used.EECs in aquatic environmental l use geographic areas. Uses in areas occurring in sensitive

locations (close proximity to aquatic environments and high runoff potentials) could result in increased risk to these organisms.

4. Surrogates were used to predict potential risks for species with no data (i.e., reptiles and amphibians). It was assumed that use of surrogate effects data are sufficiently conservative to apply the broad range of species within taxonomic groups. If other species are more or less sensitive to topramezone and/or its metabolites than the surrogates, risks may be under- or over-estimated, respectively.

5. The long term effects to wild mammals is not known. Topramezone caused thyroid tumors in rats. In addition, eye effects, pancreatic effects, and skeletal variations were identified. These effects are typically caused by inhibition of the 4-HPPD enzyme. Topramezone inhibits the 4-HPPD enzyme.

V. Literature Cited

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Open Literature (Peer Reviewed Journals)

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