MEMORANDUM

7 May 2001

Subject: Mesotrione herbicide (PC 122990): Transmittal of the new chemical review for weed control in corn (DP Barcodes: D253844, D259964, D268681) Zeneca/Syngenta, Inc.

From: Alex Clem, Environmental Scientist, ERB 3/EFED
James Goodyear, Biologist, ERB 3/EFED

Peer Review: Douglas Urban, Senior Scientist, ERB 3/EFED
Henry Craven, Biologist, ERB 3/EFED

Thru: Arnet Jones, Chief, Environmental Risk Branch 3
Environmental Fate and Effects Division (7507C)

To: Joanne Miller, PM 23, and James Stone, PM Team Reviewer
Herbicide Branch, Registration Division (7505C)

Attached is our new chemical review for the herbicide mesotrione for its use in pre- and postemergence broadleaf weed control in corn and the associated environmental fate and ecotoxicity DERs. Application of mesotrione is by air or ground spray at a maximum annual application rate of 0.43 lb ai/acre. More specific use and application details are in the review.

Since RD is interested in how herbicides compare based on their risk to plants, Douglas Urban of EFED conducted a comparative ecological risk analysis of mesotrione, atrazine, halosulfuron, and isoxaflutole. The latter three herbicides are registered for use on field corn, and had recent EFED reviews. The comparison, which portrays mesotrione favorably, is also attached.

In this memorandum we briefly give our conclusions, concerns, and recommendations for mesotrione. We have not commented on a recently received third interim report (D272184, MRID 453052-01) on a prospective groundwater monitoring study (PGM), but our comments in the current review about the first and second interim reports apply. Our lengthy, general discussion in the review about inefficient extraction procedures used in the chemical method of analysis for mesotrione and metabolites in soil (see below) also apply to future PGM submissions.

CONCLUSIONS/RECOMMENDATIONS/CONCERNS

1. **For this use, we conclude that potential adverse environmental effects to terrestrial and aquatic *animals* are minimal. In contrast, all levels of concern are exceeded for nontarget terrestrial and aquatic *plants*. Nontarget terrestrial plants are at far greater risk than aquatic.**

2. Because of the *required* use of adjuvants for effective weed control, we cannot fully assess risk to nontarget plants until limited terrestrial and aquatic plant growth tests

[§123-1(a)/(b), 123-2] are conducted with a typical end-use product (formulation mixed with selected adjuvants). With results of these tests, more realistic endpoints and possible mitigation measures (such as runoff/erosion and spray-drift buffers) could be determined. Therefore, we recommend that the registrant conduct the limited phytotoxicity studies we indicate in the review.

3. An apparent inconsistency between the fata data and the product label concerns us. According to the label, rotational crop restrictions in some cases are 120 days and longer. Such relatively long plant-back intervals imply a long-lasting residual activity for mesotrione. This is contrary to our expectations based on lab and field studies which indicate that mesotrione is relatively short-lived in soil. To make certain we are not underestimating risk, we need an explanation for the inconsistency. Perhaps the plant-back intervals were merely precautionary during the early stages of product development, or perhaps other factors such as product formulation/adjuvants, soil pH, or soil moisture conditions significantly slow degradative processes. Or, is it possible that residual activity may be caused by known or unknown degradates or metabolites?

4. Analytical Method Concern: The registrant should improve the extraction efficiency in their analytical method for determining mesotrione and metabolites in soil. Although the EPA lab verified that the submitted soil method for mesotrione and degradates is ostensibly satisfactory, after reviewing numerous studies that were performed for the registrant by different laboratories that used various extraction methodologies, we have concluded that the registrant's submitted extraction method needs to be improved. The method does work for *freshly spiked* soil/sediment samples, but not well enough for *aged* samples. The EPA lab used freshly spiked soils for the method validation; therefore, the validation was insensitive to the effects of aging. We provide a general description of this problem in the review and a lengthy, more complete one in an appendix of the review.

EFED posits that the reason for the previously mentioned, long plant-back intervals required by the proposed product label may be because of the presence of active concentrations of residual mesotrione and/or degradates (known or unknown) in soil. These older or aged residues would be analyzed as having lower than the actual concentrations or not be detectable at all unless extraction of aged samples is more efficient. This potentially impacts exposure and availability of mesotrione and degradates to the biota. This is a problem that the registrant can easily remedy by reviewing their existing data, as we put forth in the review. Adequate analytical methodology is essential for any chemical. Otherwise, in the event of an adverse incident or inadvertent contamination, there can be neither freedom from implication nor attribution of cause.

5. Remaining Data Requirements: *Except* for items 2, 3, and 4 above and submission of the final PGM report, all other environmental fate and ecotoxcity data requirements are satisfied at this time.

LABELING

The following statements should be included in the "ENVIRONMENTAL HAZARDS" labeling:

For Manufacturing-use Products

"Do not discharge effluent containing this active ingredient into lakes, streams, ponds, estuaries, oceans, or other public waters unless this product is specifically identified and addressed in an NPDES permit. Do not discharge effluent containing this product into sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of EPA."

For end-use products

"Do not apply directly to water or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when disposing of equipment wash-water or rinsate."

Surface Water Advisory

"This product may contaminate water through drift of spray in wind. This product has a high potential for runoff for several weeks after application. Poorly draining soils and soils with shallow water tables are more prone to produce runoff that contains this product. A level, well-maintained vegetative buffer strip between areas to which this product is applied and surface water features such as ponds, streams, and springs will reduce the potential for contamination of water from runoff. Runoff of this product will be reduced by avoiding applications when rainfall is forecasted to occur within 48 hours. Sound erosion control practices will reduce this product's contribution to surface water contamination."

Ground-Water Advisory

"This chemical has properties and characteristics associated with chemicals detected in ground water. Use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in groundwater contamination."

Spray Drift Advisory--Use current standard language.

Endangered species Advisory

The Agency's level of concern for endangered and threatened terrestrial plants and vascular aquatic plants is exceeded for the proposed use of mesotrione on corn. The registrant must provide information on the proximity of Federally listed terrestrial plants and vascular aquatic plants to the proposed use sites. This information may best be provided via the FIFRA

Endangered Species Task Force (Pesticide Registration [PR] Notice 2000-2), but may be produced independently, providing the information is of sufficient quality to meet FIFRA and Endangered Species Act requirements. The information will be used by the OPP Endangered Species Protection Program to develop recommendations to avoid adverse effects to listed species.

Label "Oddities"

One of our staff scientists, Norman Birchfield, has coincidentally noticed some peculiarities/discrepancies on the label that Syngenta faxed to you on 20 Mar 2001. We copy below (in distinctive e-mail type font) an edited version of the contents of the e-mail he provided. Referring to the label, he calls to your attention the following:

Page 7 states that restrictions stated related to drift of the product do not apply to forestry use, public health use, or dry formulations, but I don't think mesotrione is being proposed for any of these purposes.

Page 7 and 8 state the distance of the outermost nozzles on the boom must not exceed 3/4 the length of the wingspan or rotor, but on p11 it says boom length should only be a maximum of 70% of the wingspan.

The drop size categories "medium" and "coarse" on page 11 should specify the ASAE 572 definitions of drop size.

The final paragraph on page 11 makes no sense to me. If they want to keep the part after the colon, they should also state that crops treated with OPs or carbamates are more sensitive to the herbicidal effects of mesotrione.

The use rates stated on page 10 are very confusing. Just try and figure out how much you can apply pre and post versus only pre or only post!

Norman also pointed out that Page 6 states complete death of weeds may take up to two weeks, the duration of the phytotoxicity studies. Therefore, if some of the plants in the studies are slow to respond during that time period, toxicity could be underestimated.

Attachment to Transmittal Memo for Mesotrione Section 3

EFED's Comparative Ecological Risk Analysis for Four Herbicides Used on Corn

Executive Summary

Mesotrione, a systemic, pre-emergent and post-emergent herbicide proposed for use in field corn, was compared to three alternative herbicides - atrazine, halosulfuron and isoxaflutol. Based on this comparative analysis, halosulfuron posed the greatest risk to non-target plants, followed by isoxaflutole. Mesotrione posed the lowest risk to non-target plants, slightly less than that for atrazine. The sensitivity analysis resulted in no significant change in the relative ranking of the herbicides.

Background

Mesotrione is a systemic, pre-emergent and post-emergent herbicide proposed for the selective contact and residual control of annual broadleaf weeds in field corn. It was approved by the OPP reduced risk committee as a reduced risk pesticide warranting expedited review. The EFED screening level review of the Section 3 application for registration concluded minimal risk to mammals, honey bees, birds, fish and aquatic invertebrates because no LOCs were exceeded. However, mesotrione is highly toxic to aquatic and terrestrial vascular plants, and non-target plant LOCs were exceeded for acute risk to non-endangered and endangered plants. All herbicides are toxic to non-target plants. Since RD was interested in how herbicides compare based on their risk to plants, EFED conducted a comparative risk analysis of mesotrione, atrazine, halosulfuron, and isoxaflutole. The latter three herbicides are registered for use on field corn and had recent EFED reviews. The results of this analysis should provide some perspective on the relative risk of mesotrione to plants.

Methods

During the screening level risk assessment, EFED calculates five risk quotients (RQs) to estimate the risk to non-target plants. These RQs were used as the criteria for this comparison.[1] EFED did not include specific criteria for persistence or mobility except as

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[1] (1) RQ for risk to non-target plants due to drift is based on an EEC for drift (1% of application rate for ground application) divided by the vegetative vigor EC25 for the most sensitive species; (2) RQ for risk to aquatic non-vascular plants is based on a PRZM/EXAMS model EEC (or in the case of mesotrione, a GENEEC model EEC) divided by an EC50 for the most sensitive algal or diatom species tested; (3) RQ for risk to aquatic vascular plants is based on a PRZM/EXAMS EEC (or in the case of mesotrione, a GENEEC model EEC) divided by a *Lemna gibba* (duckweed) EC50; (4) RQ for risk to terrestrial plants on dry areas is based on an EEC for a dry adjacent area (5% sheet runoff and 1% drift for ground application) divided by a seedling emergence EC25 for the most sensitive species tested; (5) RQ for risk to terrestrial plants on semi-aquatic areas, based on an EEC for semi-aquatic areas (5% channel runoff x 10 acres and

they were included in the aquatic exposure models. Similarly, degradate toxicity and risk were also not included in this analysis. A sensitivity analysis was performed with each RQ value reduced by 90% and also increased by 90% to determine if the changes resulted in any change in the relative ranking of the analysis.[2]

As much as possible, the application methods (ground) and timing (pre-plant) were standardized so that the calculated exposures were comparable among the herbicides. Current maximum label rates for a single application were used, and similar exposure model results were chosen. The aquatic EECs were all based on PRZM/EXAMS model runs except those for mesotrione which were from GENEEC. The endpoint values for the most sensitive species tested were selected from the most recent EFED risk assessments and verified and updated by a review of the most recent DERs in EFED files.

The summary calculations are based on the simple multi-attribute rating technique (SMART)[3]. This technique was developed approximately 30-years ago and has become a standard in decision modeling. It prescribes that: (1) each herbicide be rated on each RQ, (2) each RQ be assigned a measure of importance to the decision-maker (in this case all RQs have been set at the same measure of importance, high), and (3) a summary score for each herbicide be calculated as a weighted average of the RQs. Thus, the higher the summary score, the higher the risk. The result of this process has proven to be superior to the alternative of reliance on intuition.

The basic equation used to calculate the summary values for the comparison is as follows:

$$\text{Summary Value}_{(\text{scale from 0 to 10})} = \sum [\![(RQ_i)(RQ_{max})^{-1}]\!] [\![(\text{Weight})(\sum \text{Weights})^{-1}]\!] (10)$$

where RQ_i is the RQ for one of the five non-target plant risk calculations for an herbicide and RQ_{max} is the maximum RQ for that calculation all herbicides; Weight is the

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1% drift for ground application) divided by a seedling emergence EC25 for the most sensitive species tested.

[2] One of the greatest sources of uncertainty in the calculation of these RQs is the estimate of terrestrial exposure since it is based on percentages of the application rates with no consideration given to environmental degradation and dissipation. The aquatic exposure estimates do include environmental fate parameters and provide a better estimate environmental exposure. Assuming that the magnitude of the differences in exposure approximate the magnitude of the differences in the terrestrial environment, we took the ratio of the application rate to the aquatic EEC and normalized it to 1 lb ai/A for each herbicide. Then, we calculated the percentage difference between the largest and smallest ratio, which equaled ~ 90%. This percentage, then, was used in the sensitivity analysis to represent a major source of uncertainty in the RQ estimates.

[3] See the following reference for a more detailed explanation of the underlying algorithms: Goodwin, P. and G. Wright. 1998. Decision analysis for management judgement, 2nd Ed. John Wiley & Sons, England. pp.454.

importance value placed on each criterion, with high = 10, medium = 5, and low = 3.33; and, $\sum$Weights is the sum of all the weights for all the RQs.

Results

The decision table and graphs below provide visual expressions of the comparative analysis. They show the risk quotients, the summary values, the relative ranking of the herbicides based on sum of the weighted average RQs, and the results of the sensitivity analysis:

Table 1. Decision Table for Comparative Analysis basd on RQ Values

	Risk to Vascular Plants due to Drift Alone	Risk to Aquatic NonVascular Plants	Risk to Aquatic Vascular Plants	Risk to Terrestrial Plants on Dry Areas	Risk to Terrestrial Plants on Semi-Aquatic Areas	Summary
Halosulfuron		13.64	35.70	94.50	6615.00	8.11
Isoxaflutole	200.00					2.69
Atrazine						
Mesotrione						

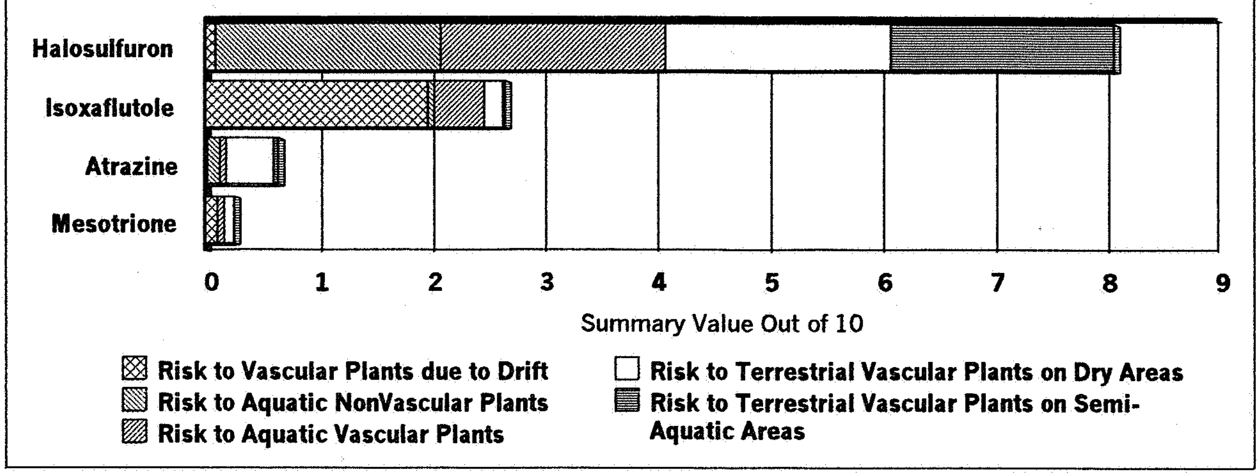
Risk Quotients

Highest Risk	Highest RQ
Medium Risk	50 to 75% of Highest RQ
Low Risk	25 to 49% of Highest RQ
Lowest Risk	

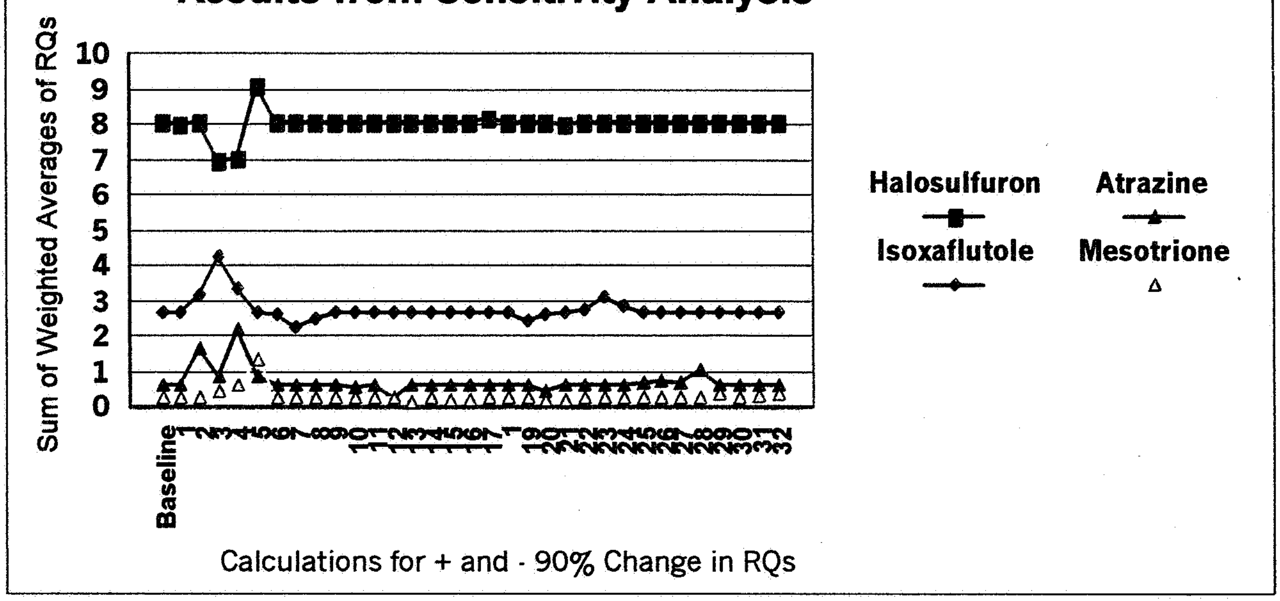
Summary

Highest Risk	10.00 to 7.50
Medium Risk	7.49 to 5.00
Low Risk	4.99 to 2.50
Lowest Risk	

Graph 1.
Sum of Weighted Averages of RQs



Graph 2.
Results from Sensitivity Analysis



Interpretation of Results

The calculation of RQs for the screening level non-target plant risk assessments involves the use of conservative estimates of exposure and toxicity. Thus, the RQ values could range considerably lower. A probabilistic risk assessment could characterize this range by analyzing the variation in each term of the RQ, i.e., the plant toxicity values as well as the modeled exposure estimates. However, such an analysis would require time and resources beyond those available for this comparative analysis.

As previously mentioned, EFED did not include specific criteria for persistence or mobility (except as they were included in the aquatic exposure models), nor for degradate toxicity and risk, or plant incident reports. Consideration of such information is usually provided in an environmental risk characterization. With such consideration, the overall risk ranking of these herbicides could change.

This present analysis incorporates a number of important assumptions, which, if eventually proven false, could yield far different results:

> * the five RQ values calculated for non-target plants are good screening estimates of the risk from the use of herbicides to non-target plants;
> * the use of the SMART technique is useful and appropriate for comparing herbicides based on RQs;
> * the sensitivity analysis, as performed, captures the likely changes in the summary values (sum of the weighed averages of the RQs);
> * the use of 90% in the sensitivity is an appropriate estimate of the variation in a single RQ value.

Conclusions

The assumptions and methods used in this analysis are reasonable. Thus, the results provide a good approximate risk ranking of these four herbicides.

Mesotrione posed the lowest risk to non-target plants, slightly less than that for atrazine. The sensitivity analysis resulted in no significant change in the relative ranking of the herbicides.

Douglas J. Urban, Senior Scientist, ERB 3, EFED

May 3, 2001

ENVIRONMENTAL FATE AND EFFECTS DIVISION
ENVIRONMENTAL RISK BRANCH III

NEW CHEMICAL REVIEW (SECTION 3)
FOR THE USE ON CORN OF THE HERBICIDE

MESOTRIONE

(PC 122990, CAS No. 104206-82-8)

3 May 2001

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CHAPTER I

INTEGRATED ENVIRONMENTAL RISK CHARACTERIZATION AND CONCLUSIONS

USE SUMMARY
(Additional important information and restrictions given in next chapter)

Mesotrione, according to the proposed label for the formulation ZA1296 4-SC, is a systemic, preemergence and postemergence herbicide for "the selective contact and residual control of annual broadleaf weeds in corn" (all varieties of field corn, but not sweet corn). Most grass weeds are not controlled effectively. The product is said to be absorbed through the soil by emerging weeds and through the foliage of emerged weeds.

Weed growth ceases soon after application, while death of the weeds may take up to two weeks. Dry conditions may reduce the effectiveness of preemergence applications. An activating rain (0.5") is usually required within 7-10 days following application; otherwise, rotary hoeing is suggested. Its action is not affected by rain falling one hour or more after application to weed foliage.

Application Rate - According to the originally proposed label, mesotrione application was to vary from 0.18 to 0.27 lbs ai/acre preemergence and up to 0.16 lbs ai/acre postemergence, with a maximum total of 0.43 lbs ai/acre per season. No more than two applications were to be made per season. No interval between the two applications was given. However, a modified, proposed label for the product CALLISTO, which Jim Ridsdale of Syngenta sent by Fax on 20 Mar 01 to Jim Stone and Jim Tompkins of the Registration Division, specifies an application interval of at least 14 days between the two applications. Additionally, there is an offsetting minor difference of 0.03 ai lb/acre in application rates as follows: 1) the preemergence rate has gone *down* from 0.27 to 0.24 lb ai/acre, and 2) the postemergence rate gone *up* from 0.16 to 0.19 ai lb/acre. The offsetting change does not appreciably alter our assessment for mesotrione. The sum remains the same 0.43 ai lb/acre, and is the primary basis of our assessment.

Mesotrione will be applied preemergence by ground equipment, and by air or ground equipment postemergence. Postemergence applications should be made when annual broadleaf weeds are at the 3-8 leaf stage of corn growth (total leaves). Corn up to 30" tall may be treated. Broadleaf weeds up to 18" tall are said to be controlled.

ECOLOGICAL TOXICITY AND RISK ASSESSMENT

Abstract. *Potential risk of mesotrione to animals is low. For nontarget terrestrial plants and vascular aquatic plants, all levels of concern are exceeded. Nontarget terrestrial plants are at far greater risk than aquatic.*

Terrestrial Environment

Mammals - Mesotrione had a white rat LD50 of >5,000 mg/kg, and is therefore considered to be practically nontoxic acutely to wild mammals. The degradates MNBA and AMBA are also practically nontoxic on an acute basis. The estimated reproductive LOAEL for mesotrione was 2,000 ppm. No mesotrione risk quotients exceed the level of concern (LOC). The potential acute and chronic risk to wild mammals is low.

Birds - Mesotrione is considered practically nontoxic to birds. It has an acute oral LD50>2,000 mg/kg and a dietary LC50 >5,000 ppm for bobwhite quail. There is a difference between the reproductive study NOAECs of the bobwhite quail (3,000 ppm) and the mallard duck (1210 ppm).

Maximum EEC values for short grass resulted in RQs that did not exceed the LOCs for acute reproductive risk to birds. Based on submitted studies, the potential acute and chronic risk of mesotrione to birds is low.

Bees - Mesotrione has an acute contact toxicity of >100 micrograms/bee, and an acute oral toxicity of >11 micrograms /bee. These values indicate a low potential risk to honey bees.

Plants - For Tier II *seedling emergence,* lettuce is the most sensitive dicot with EC25 and EC05 values of 0.0033 and 0.0012 lb ai/acre, respectively; onion is the most sensitive monocot with EC25 and EC05 values of 0.032 and 0.001 lb ai/acre, respectively.

For Tier II *vegetative vigor,* tomato is the most sensitive dicot with EC25 and EC05 values of 0.00023 and 0.0001 lb ai/acre, respectively; onion is the most sensitive monocot with EC25 and EC05 values of 0.0009 and 0.0001 lb ai/acre, respectively .

For all application scenarios for mesotrione, endangered and nonendangered acute levels of concern are exceeded for monocots and dicots in dry and semi-aquatic areas using the seedling emergence and vegetative vigor toxicity data. An exception is for monocots in a dry area for either single applications (aerial or ground) or for two ground applications using monocot seedling emergence data. The endangered species acute RQs for monocots ranged from 11 to 219. Comparable to monocots, the endangered species acute RQs for dicots ranged from 9.5 to 215. The nonendangered species acute RQs for monocots ranged from 0.4 to 24. The nonendangered species RQs for dicots ranged from 3.5 to 107. Currently, there are no separate criteria for chronic risk to plants.

EFED's assessment shows that mesotrione may kill nontarget terrestrial plants when misapplication, drift, or runoff brings it to field borders and into adjacent fields.

This loss of plants could thin the ground cover and reduce the supply of food and cover for animals. Therefore, the population size of vertebrates and invertebrates could be affected.

Aquatic Environment

Fish - Mesotrione is practically nontoxic to fish with acute LC50 values ranging from 120 ppm (bluegill sunfish & rainbow trout) to 410 ppm (sheepshead minnow). The chronic toxicity value is 16 ppm (MATC for fathead minnow). When using the GENEEC modeled EEC of 20 ppb, all RQs are less than 0.01. Based on the submitted studies, the potential acute and chronic risk of mesotrione to fish is low.

Aquatic Invertebrates - The acute toxicities of mesotrione to *Daphnia magna* (48-hr LC50 = 900 ppm), the mysid shrimp (48-hr LC50 = 3.3 ppm), and the eastern oyster (48-hr LC50 = 72 ppm) categorize it as practically nontoxic to moderately toxic. The acute toxicities of the degradates MNBA and AMBA to *Daphnia magna* (48-hour EC50) are 130 mg/L and 160 mg/L, respectively. The chronic *Daphnia magna* toxicity of mesotrione (21-day MATC = 230 ppm) indicates low toxicity. All mesotrione RQs are less than 0.01 when the GENEEC model is used to determine the EECs. The potential acute and chronic risk of mesotrione to aquatic invertebrates is low as indicated by risk quotient calculations and comparisons to LOCs.

Plants - *Navicula pelliculosa* is the least sensitive alga to mesotrione (120-hr EC 50 = 68 ppm) and *Selenastrum capricornutum* (=*Kirchneria subcapitata*) is the most sensitive alga (120-hr EC 50 = 1.9 ppm; RQ < 0.01). The LOC for a green alga was not reached. There are no endangered algae.

The only vascular aquatic plant tested was *Lemna gibba* (14-day EC50 = 0.018 ppm). At the multiple application rate, the RQs for nontarget and endangered plants are 1.1 and 2.7, respectively, exceeding the LOC criterion of 1.0.

Mesotrione is toxic to vascular aquatic plants, but not to nonvascular aquatic plants (algae) at proposed application rates. If mesotrione is added to a body of water inadvertently, by drift or by runoff, it could reduce the mass of aquatic vascular plant life and the biomass of the animals that depend upon those plants.

DRINKING WATER RESOURCES

Drinking water screening concentrations for humans potentially exposed to mesotrione in surface water (estimated from the GENEEC tier 1 environmental screening model, version 1.2, 5/3/95) and ground water (estimated from the SCI-GROW Regression Model, Version 1.0, 11/12/97) are:

Surface Water	Acute (Instantaneous) Exposure:	**20 µg/L** (parts per billion or ppb)
	Chronic (56-Day) Exposure:	**13 µg/L** (parts per billion or ppb)
Ground Water	Acute and Chronic Exposure:	**0.15 µg/L** (parts per billion or ppb)

For coarse screening purposes, combined concentrations of MNBA and AMBA are expected to be less than roughly 30 to 40% (50 to 60% in molar equivalents) of those tabulated above for parent mesotrione. However, because there is a large uncertainty about the persistence of AMBA under anaerobic conditions and perhaps at lower pHs, groundwater concentrations of AMBA could be several times higher.

CHAPTER II

INTRODUCTION

Use Characterization, Chemical Class, Mode of Action, Crop Restrictions Additional Comments/Recommendations

Mesotrione, according to the proposed label for the formulation ZA1296 4-SC, is a systemic, preemergence and postemergence herbicide for "the selective contact and residual control of annual broadleaf weeds in corn" (all varieties of field corn, but not sweet corn). Most grass weeds are not controlled effectively. The product is said to be absorbed through the soil by emerging weeds and through the foliage of emerged weeds.

Mesotrione is a tri-ketone that, according to the registrant, inhibits specifically the enzyme p-hydroxyphenylpyruvate dioxygenase (HPPD). This disrupts the pigment (chlorophyll) biosynthesis pathway in susceptible plants.

The proposed maximum seasonal use rate of 0.48 kg ai/ha (0.43 lb ai/acre) may be divided into no more than two applications with at least a 14-day application interval. The maximum preemergence rate is 0.30 kg/ha or 0.27 lb/acre (0.24 lb/acre on revised, proposed label). The maximum postemergence rate is 0.18 kg/ha or 0.16 lb/acre (0.19 lb/acre on revised, proposed label). Application is by aerial or ground spray. Application to annual broadleaf weeds is to be at the 3-8 leaf stage of corn growth. Corn up to 30 inches tall may be treated. Broadleaf weeds up to 18 inches tall are said to be controlled. Preemergence application requires an activating rain/irrigation (0.5 inches) within 7-10 days; otherwise, rotary hoeing is suggested.

Adjuvants (nonionic surfactants plus crop oil concentrate or methylated seed oil) and added urea (UAN, 28-0-0) are required for postemergence use. In addition to these additives, tank mixtures of mesotrione with various other herbicides may be used. *Because of the use of adjuvants and potential concern for nontarget phytotoxicity, EFED is requesting limited, additional testing of an end-use product with selected adjuvants as a condition for registration.* Testing could include, for example, vegetative vigor and seedling emergence(123-1a/b) with three terrestrial test species: onion, tomato, and lettuce; and an aquatic test (123-2) with duckweed. The test material would be the end-use product with surfactant and other adjuvant(s) that the registrant believes will be most commonly used with ZA 1296 4-SC. The need for any additional plant testing is reserved pending the results with onion, tomato, lettuce, and duckweed.

Rotational crop restrictions on the proposed label are given as: 1) a 30-day interval before planting soybeans and sorghum; 2) a 120-day wait for small grains, alfalfa, and clover; and 3) planting of all other rotational crops and tobacco must wait until the spring following application. *The relatively long plant-back intervals of 120 or more days imply a* *long-lasting residual activity, contrary to EFED's expectations based on lab and field studies that show mesotrione to be relatively short-lived in soil. The registrant should address this apparent inconsistency.* Perhaps the plant-back intervals were merely precautionary during the early stages of product development, or perhaps other factors such as product formulation, soil pH, or soil moisture conditions significantly slow degradative processes. Or, is it possible that residual activity may be caused by known or unknown degradates or metabolites?

CHAPTER III

ENVIRONMENTAL FATE ASSESSMENT

A. Status of Environmental Fate Data

In applying for this new chemical registration, the registrant has submitted laboratory study data for mesotrione on more soils (20) than the reviewer can recall. The Agency applauds the use of a spectrum of soils. There are also key studies for two metabolites, AMBA and MNBA. Without these "extra" laboratory data for parent and metabolites, the environmental fate assessment of mesotrione would have been seriously incomplete and possibly incorrect.

Although many of the individual environmental fate studies had shortcomings which prevented them from being fully satisfactory, taken as a whole, the Agency can adequately assess the environmental fate of mesotrione[1]. Overall, the environmental fate data requirements for use of the herbicide mesotrione on corn are *satisfied*, except for: 1) field spray-drift and spray droplet-size spectra, and 2) analytical methods in soil and water (the existing soil method is an important, but easily remedied, concern). Discussion on these two remaining requirements follows.

Regarding the spray-drift related requirements, the registrant is a member company of the Spray Drift Task Force (SDTF). As a member, the registrant may be able to satisfy this requirement through data which the SDTF has submitted to the Agency.

The analytical method for determining mesotrione and the metabolites MNBA and AMBA in *water* is currently pending validation by the EPA laboratory. We anticipate, based on EPA lab validation results that we have already received on *soil*, that the water method should be satisfactory. However, even though the EPA lab verified that the submitted *soil* method for mesotrione and degradates is ostensibly satisfactory, *the registrant needs to re-investigate extraction procedures for soil.*

After reviewing studies that were performed for the registrant by different laboratories which used various extraction methodologies, EFED has concluded that *freshly spiked* soil/sediment samples are easily extracted by using any of several methods (including an abbreviated procedure that the registrant has proposed). However, the fate studies also showed that extraction efficiency declined significantly with progressive aging (more than three days, roughly). We provide a lengthy general description of this problem, and make

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[1]Data Evaluation Reports (DERs) with their summaries/conclusions for all of the many submitted studies are available in EFED files. However, the reader or future fate reviewers are cautioned that, because of specific study shortcomings, their partial nature, the existence of several closely related series of studies, and the pH dependence of mesotrione and degradates, the DERs <u>cannot</u> be used in isolation, but must be taken in the context of all submitted data.

comparisons of extraction differences we observed in various environmental fate studies in Appendix C of this document. Evidence of extraction concerns as they emerged are also provided in various Data Evaluation Reports (DERs) for submitted fate studies. The EPA lab validation procedure used freshly spiked soils, and, therefore, was insensitive to the effects of aging. EFED also conjectures that the reason for the previously mentioned, long plant-back intervals required by the proposed product label may be because of the presence of active concentrations of residual mesotrione and/or degradates in soil. These older or aged residues would be analyzed as having lower than the actual concentrations or not be detectable at all unless extraction of aged samples is more efficient. This is potentially a serious problem concerning exposure and availability of mesotrione and degradates or metabolites to the biota, a problem that the registrant can easily remedy by reviewing their existing data, as we have indicated here and in Appendix C.

B. Environmental Fate Assessment

In addition to the summary below and the more detailed assessment which follows the summary, Appendix B provides both complementary and supplementary descriptions and considerations for selected environmental fate study results by Guideline category. Specific procedural details for the selected studies as well as other reviewed studies are available in DERs for separate study submissions, but, as footnoted previously, because of the chemical nature of mesotrione and study particulars, individual studies cannot be used in isolation.

Summary. The herbicide mesotrione and its major metabolites MNBA and AMBA are distinctly acidic compounds. This acidic/ionic property has a major influence on their behavior in environmental media at different pHs. As a suite, these compounds had low to virtually no sorption to tested soils/sediments at the more neutral pHs typical of agriculture, indicating high potential for leaching and runoff. Tending to offset the opportunity for leaching and runoff, parent was relatively short-lived. Generally, MNBA and AMBA were also relatively short-lived under aerobic conditions. However, as indicated further below, there is greater uncertainty about the persistence of MNBA and AMBA under suboxic conditions, such as would be found in subsoil and ground water. These metabolites would be more likely candidates for leaching and runoff than parent. Based on physicochemical properties, bioconcentration of mesotrione, MNBA and AMBA is not expected. Likewise, volatilization of mesotrione and its transformation products (except for carbon dioxide) is not indicated.

Based on laboratory studies, the primary routes of environmental transformation for parent mesotrione are aerobic and suboxic metabolism in soil and water. Numerous laboratory "half-lives" (more than 17) ranged from around four days to one month, depending on ambient conditions, especially pH (see main text). In relative, practical terms, photolysis is a minor degradative route. Mesotrione was stable against simple hydrolysis.

Sorption of mesotrione to soil organic matter and its aerobic soil metabolism half-lives (paired values for sorption and half-life for 17 soils) each correlate inversely with pH–the higher the pH, the lower the apparent sorption to soil organic matter and the shorter the half-life (see main text). Lower sorption to soil acts to increase available concentrations, while shorter half-lives act to decrease them. For mesotrione, the overall quantitative effect tended to normalize estimated environmental concentrations to a central value, regardless of pH.

Only three compounds, MNBA, AMBA, and carbon dioxide, were identified specifically as by-products in laboratory studies. Depending on conditions and time after application of parent, MNBA and AMBA can comprise up to approximately 60% of applied parent equivalent. Aerobic conditions favor MNBA, suboxic conditions favor AMBA. Half-lives for MNBA can only be crudely estimated from the available data and are highly uncertain. In at least two aerobic soils, MNBA half-lives appeared to be measured in one to several months, but seemed to be much shorter in others. Although, as for parent, metabolism rates for MNBA may show correlation with pH, this has not been pursued because of lack of sufficient, amenable data.

In a separate aerobic soil metabolism study with AMBA as the test substance in three soils, AMBA half-lives averaged 21 $\pm$ 5 days with an upper 90% confidence interval on the mean of 31 days. Data are insufficient to determine the range of variation of half-life with pH. Under suboxic conditions, half-lives for AMBA cannot be reliably established because of study deficiencies; a crude, reviewer-estimated first-order half-life for AMBA under the existing study conditions is 110 days, but may be longer with greater restriction of oxygen.

Under aerobic conditions, carbon dioxide was a ubiquitous product that issued from key positions in both rings of the mesotrione molecule. The cyclohexanedione ring was much more reactive in yielding carbon dioxide than the benzene ring. In some cases, carbon dioxide comprised up to about 80% of the radioactive dose after about six months. Increasingly difficult to extract soil residues tended to increase with time up to roughly15 to 50% of the dose, and then tended to decrease in roughly complementary fashion with increasing levels of carbon dioxide. This pattern clearly indicates progression to ultimate degradation/mineralization when there is sufficient aeration. However, when aeration was limited (suboxic conditions), carbon dioxide was only sparingly evolved from either ring. Under such conditions, as stated above, AMBA was a prominent metabolite that may be persistent when oxygen is in short supply.

Three terrestrial field dissipation studies on bare ground did not adequately account for the dissipation of mesotrione. They did, however, provide supplemental aspects that are consistent with the laboratory findings of a relatively short residency time for mesotrione in soil. The registrant failed to identify any degradates in the field, or to clearly determine leaching potential.

The registrant has also submitted (without request from the Agency) two interim reports on a prospective groundwater monitoring (PGM) study at a site in Michigan. So far, superficial indications are that no leaching of *parent* was occurring. However, it is not clear whether there was actually a lab separation step and analysis for the transformation products MNBA and/or AMBA, which would be likely candidates for leaching. There is also a potential problem with soil extraction efficiency. The registrant should clarify these uncertainties in the final PGM report. Additionally, soil and groundwater pHs were typically between 7and 8, where, according to the laboratory data, transformation of mesotrione to metabolites would be more rapid. Until the registrant submits a final report with study details and actual laboratory sequences for parent *and metabolites* in the PGM study, we cannot project general leaching conclusions. If there are human health concerns for MNBA and/or AMBA exposure, then potential concentrations of these compounds should be considered in the drinking water exposure assessment.

Drinking water screening concentrations for humans potentially exposed to mesotrione in surface water (estimated from the GENEEC tier 1 environmental screening model, version 1.2, 5/3/95) and ground water (estimated from the SCI-GROW Regression Model, Version 1.0, 11/12/97) are:

Surface Water	Acute (Instantaneous) Exposure:	**20 µg/L** (parts per billion or ppb)
	Chronic (56-Day) Exposure:	**13 µg/L** (parts per billion or ppb)
Ground Water	Acute and Chronic Exposure:	**0.15 µg/L** (parts per billion or ppb)

For coarse screening purposes, combined concentrations of MNBA and AMBA are expected to be less than roughly 30 to 40% (50 to 60% in molar equivalents) of those tabulated above for parent mesotrione. However, because there is a large uncertainty about the persistence of AMBA under anaerobic conditions and perhaps at lower pHs, groundwater concentrations of AMBA could be several times higher.

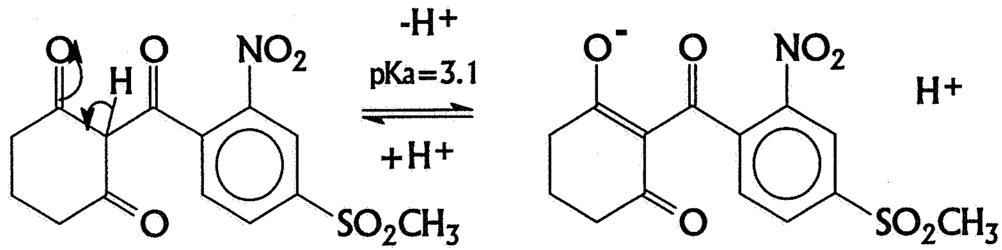
Physicochemical Nature of Mesotrione and Relationship to Environmental Fate

As can be seen by inspection of the chemical structures given below and from the separate table of physicochemical properties (Table I) which follows, mesotrione is an acidic herbicide with prominent sulfonyl and nitro groups. As can also been seen from the given chemical structures of the identified metabolites MNBA and AMBA, these are benzene ring-based acids that remain after the connection to the cyclohexanedione ring is broken. MNBA and AMBA also retain the sulfonyl functional group. Selected physicochemical properties for MNBA and AMBA are given in Table II.

Chemical Structures and Identification of Mesotrione (ZA 1296) and the Metabolites MNBA and AMBA

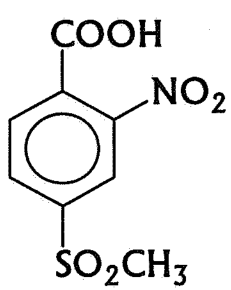
Chemical Name: 2-[4-methylsulfonyl-2-nitrobenzoyl]-1,3-cyclohexanedione
Chemical I.D. Numbers: EPA PC Code 122990, CAS No. 104206-82-8
Empirical Formula: $C_{14} H_{13} O_7 N S$
Molecular Weight: 339.3 g/mol

Structure of Mesotrione (associated and dissociated forms)



Structure of Identified Metabolites

MNBA	AMBA
4-(methylsulfonyl)-2-nitrobenzoic acid	2-amino-4-(methylsulfonyl)benzoic acid
(CAS No. 110964-79-9)	(CAS No. Not Available)



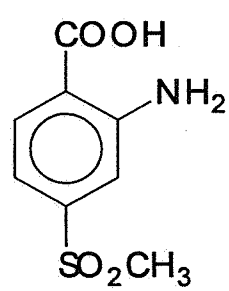


TABLE I

Physicochemical Properties of Mesotrione for Indicated Purities (from Product Chemistry Review by Harold Podall, 24 Feb 2000; D263245)	
Physical State	96.7% a.i.: opaque solid
Melting Point/Melting Range	96.7% a.i.: 148.7° - 152.5° C
Relative Density/ Bulk Density	96.7% a.i.: relative density: 1.46 g/ml at 20° C bulk density: 0.56 g/ml at 23.3° C
UV/Visible Absorption	99.3% a.i.: UV absorption maximum in methanol at 256 nm with a molar extinction coefficient of 2.24×10^4 L/(mole·cm)
Dissociation Constant in Water	99.7% a.i.: pKa = 3.12 at 20° C
pH	96.7% a.i.: 3.4 (for a 1% by wt. dispersion in water) at 25 °C
Solubility	Solubility in water of 99.7% a.i. sample at 20° C : 160 ppm in unbuffered water 0.22 g /100ml at pH 4.8 1.5 g /100ml at pH 6.9 2.2 g / 100ml at pH 9 Solubility in organic solvents of technical (96.7% a.i.) at 20° C: 0.37 g / 100 ml methanol 1.7 g / 100 ml ethyl acetate 0.27 g / 100 ml toluene 10.4 g / 100 ml acetonitrile < 0.03 g /100 ml heptane 8.1 g / 100 ml acetone
Partition Coefficient (P_{ow}) (Octanol/Water)	99.7% a.i. sample at 20° C : log P_{ow} = 0.11 in unbuffered water log P_{ow} = 0.90 in pH 5 buffer log P_{ow} < -1 at pH 7 and 9 buffered water
Vapor Pressure	99.7% a.i.: 4.3×10^{-8} Torr (5.7×10^{-6} Pa) at 20° C Henry's Law Constant =< 5.1×10^{-7} Pa . m^3/mol at 20° C

TABLE II

Selected Physicochemical Properties of MNBA (99.6%) and AMBA (99%) at 20° C (directly or derived from MRIDs 451960-03 and 451960-02, respectively)	
Molecular Mass (g/mol)	MNBA: 245.21 AMBA: 215.22
Acid Ionization Constant in Water (Ka) and pKa	Approximate values calculated from solubility and pH in unbuffered water given in next row below: MNBA: 1.6×10^{-2} (pKa = 1.8) AMBA: 9.3×10^{-5} (pKa = 4.0)
Solubility	In water: MNBA: 4.0 mg/mL in unbuffered water (final pH 2.0) 14.2 mg/mL at pH 2.6 32.4 mg/mL at pH 2.9 (exceeds buffer capacities at higher pH) AMBA: 0.3 mg/mL in unbuffered water (final pH 3.5) 1.8 mg/mL at pH 4.7 23 mg/mL at pH 6.1
Octanol/Water Partition Coefficient (P_{ow})	MNBA: log P_{ow} = -1.3 in unbuffered water log P_{ow} = -2.6 in pH 5 buffer AMBA: log P_{ow} = 0.32 in unbuffered water log P_{ow} = -0.30 in pH 5 buffer
Vapor Pressure	MNBA: 6.4×10^{-7} Pa (4.8×10^{-9} Torr) AMBA: 4.7×10^{-7} Pa (3.5×10^{-9} Torr)
Henry's Law Constant (Calculated from vapor pressure and solubility above)	In unbuffered water: MNBA: 3.9×10^{-8} Pa-m³/mol (3.9×10^{-13} atm-m³/mol) AMBA: 3.4×10^{-7} Pa-m³/mol (3.4×10^{-12} atm-m³/mol)

The mesotrione pKa of 3.12 (see Table I above) means that it is approximately 40 times more acidic than acetic acid, the distinctive, sour component in vinegar. This acidic/ionic property has a major influence on the behavior of mesotrione in environmental media at different pHs. The dependence on pH is such that there is a high correlation between pH and sorption to soil organic matter, and a lesser, understandably more complex correlation between pH and soil "half-life." The major trends with pH for sorption and half-life are such that the lower the pH, the higher the sorption to soil organic matter and the longer the corresponding aerobic soil "half-life." In influencing environmental concentrations, these two tendencies act in opposition. The relationships are illustrated in the next table (Table III), where the data are sorted by ascending pH, and in the corresponding graphs (Figures 1 and 2) that follow the table. In the table and graphs, sorption to organic matter is calculated as sorption to organic carbon, which is quantified and symbolized by the organic carbon sorption coefficient Koc. These relationships with pH will be mentioned again in context in other parts of this document. The larger scatter (lower correlation) in half-life in different soils with similar pH is no doubt due to the nature and activity of soil microbes which depend on factors[2] not currently measured adequately in guideline studies, and which, if available, would permit normalization of half-lives among different soils and different studies. It is an interesting happenstance for mesotrione that, in the case of transport of mesotrione to water bodies or its availability in soil pore water or ground water, the opposing quantitative relationship between sorption to soil organic matter and half-life has the effect of essentially normalizing environmental concentrations in these media to a nearly central value, regardless of pH. This is illustrated in Table III by the narrow range of estimated environmental concentrations in pond water (EECs in the last two columns) as computed by the standard GENEEC environmental simulation model (described briefly elsewhere in this document) which the Agency uses for screening pesticides.

[2] For example, one important factor that differed among study submissions was soil moisture potential (matric potential or soil suction, which is a non-linear function not to be confused with percentages of soil water holding capacity) which can dramatically affect microbial activity or respiration rate, which, in turn, is affected by soil organic matter.

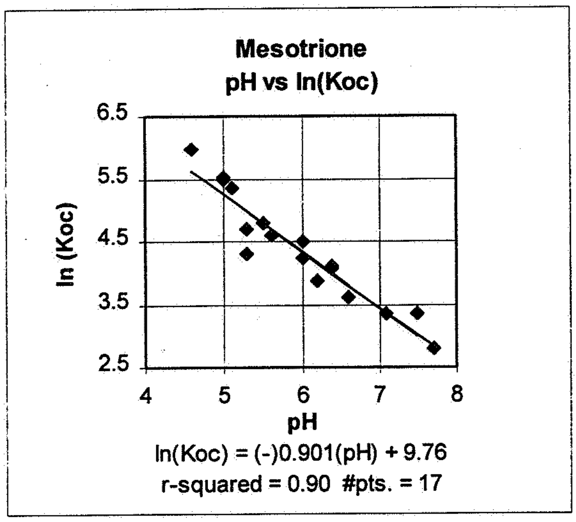
TABLE III

pH Dependence of Soil Sorption (Koc) and Aerobic Soil Metabolism Half-Life (t1/2) and Opposing Influence on GENEEC Estimated Environmental Concentrations (EEC)*

Soil #	EPA MRID#	Soil Identification	pH (in water)	Koc (Kd) (mL/g)	ln Koc	Aero. Soil t1/2 (days)	ln (t1/2)	Aero. Aq. t1/2* (days)	Geneec Acute EEC* (ppb)	Geneec Chronic EEC* (ppb)
1	44505204	Osceola NB 724	4.6	390 (2.3)	5.97	25.9	3.254	51.8	10.17	6.23
2	44505204	Noblesville IN 727	5	250 (3.4)	5.52	24.1	3.182	48.2	12.48	7.84
3	44505204	Champaign IL 741, Low pH	5	240 (5.0)	5.48	31.5	3.450	63	12.86	8.77
4	44505204	Valley Springs SD 732	5.1	210 (4.4)	5.35	15.8	2.760	31.6	13.01	7.03
5	44505204	New Holland OH 730	5.3	73 (1.3)	4.29	19.1	2.950	38.2	17.95	11.11
6	44505204	Elk City KS 725	5.3	110 (1.1)	4.70	8	2.079	16	14.79	5.52
7	44505204	Breese IL723	5.5	120 (1.0)	4.79	16.6	2.809	33.2	15.77	9.02
8	44505204	Danville IA 722	5.6	98 (1.6)	4.58	10.6	2.361	21.2	15.88	7.2
9	44505204	Martinsville IN 728	6	90 (0.68)	4.50	8.5	2.140	17	15.7	6.16
10	44505204	Delavan WI 729	6	70 (0.74)	4.25	12.9	2.557	25.8	17.49	8.99
11	44373532	Richmond WI	6.2	47.5 (0.74)	3.86	12.8	2.549	25.6	18.62	9.61
12	44505203	ERTC NC	6.4	58 (0.35)	4.06	12	2.485	24	17.94	8.89
13	44505204	Clarence MO 731	6.4	60 (0.63)	4.09	14.4	2.667	28.8	18.18	9.94
14	44505204	Land O'Lakes IA 721	6.9	37 (0.82)	3.61	22	3.091	44	20.1	13.33
15	44505203	Pickett Piece, England	7.1	29 (1.1)	3.37	4.6	1.526	9.2	16.29	3.95
16	44505204	Champaign IL 742, High pH	7.3	29 (0.61)	3.37	8.2	2.104	16.4	18.56	7.23
17	44505203	Garonne, France	7.7	16.5 (0.18)	2.80	5.9	1.775	11.8	18.1	5.46
								GENEEC EEC Ranges:	**10-20 ppb**	**4-13 ppb**
								N = 17		
								Median = Avg.:	**16 ppb**	**8 ppb**
								Avg. ± S.D.:	**16 ppb ± 3 ppb**	**8 ppb ± 2 ppb**

*GENEEC EECs were computed with the Koc and the soil and aquatic metabolism half-life values tabulated above. For each soil, a default aerobic aquatic metabolism half-life was taken as twice that of the aerobic soil half-life. All other chemical specific factors were essentially insignificant. For screening purposes, the application scenario was taken as a single application by aircraft at the total maximum annual rate of 0.43 lb/acre (without incorporation). In actuality, the application would be split, as presented in the introduction to this review; therefore, EECs would typically be slightly lower. A sample GENEEC output table for soil #14 is given as Appendix F.

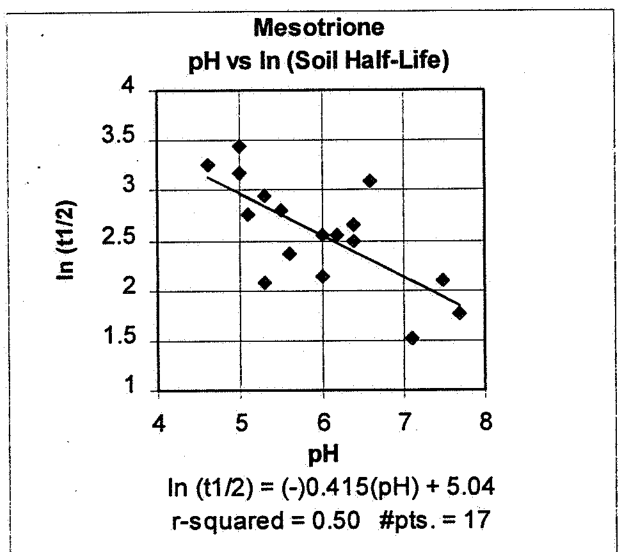
Figure 1



Regression Output:

Constant	9.76
Std Err of Y Est	0.46
X Coefficient(s)	-0.901
Std Err of Coef.	0.0769
R Squared	0.90
No. of Observations	17
Degrees of Freedom	15

Figure 2



Regression Output:

Constant	5.04
Std Err of Y Est	0.65
X Coefficient(s)	-0.415
Std Err of Coef.	0.107
R Squared	0.50
No. of Observations	17
Degrees of Freedom	15

Degradation/Metabolism/Transformation Products (see also Appendix B)

Based on laboratory studies, the *primary route of environmental transformation for mesotrione is aerobic and suboxic metabolism in soil and water.* Numerous laboratory "half-lives" (17 aerobic soil, 2 aerobic aquatic, 1 suboxic aquatic) ranged from around four or five days to around one month. Although not conclusive because suboxic data are limited to only one aquatic system with a pH of approximately 7, the degree of aeration did not appear to alter the rate of parent mesotrione metabolism.

In relative, practical terms, photolysis of mesotrione would be a minor degradative route. (The photolytic half-life in water is extrapolated to be 80 to 90 days; submitted soil photolysis data are highly uncertain.) Mesotrione was stable against hydrolysis.

Only three compounds, MNBA, AMBA (structures given previously), and carbon dioxide, were identified specifically as major by-products in laboratory studies. Unidentified and increasingly difficult to extract soil associated components and unidentified water associated (polar) components also generally comprised major portions of by-products. In more detail, results are as follows:

<u>MNBA</u> generally reached no more than 10-12% of the parent dose (typically 4 or 5%) in the soils tested, most of which were acidic. However, in three of seventeen aerobic soils with more neutral pHs (more desirable for growing corn), maximum concentrations reached approximately 30, 50, and 60% of the dose. These data indicate that MNBA would be a major product in many soils in which corn is grown. Even though the registrant attempted to estimate half-lives for MNBA from mesotrione metabolism data, EFED concludes that the available data are insufficient for the purpose. In at least two soils, MNBA "half-lives" appeared to be one to several months, but much shorter in others. There was not a separate study with MNBA alone, as there was for AMBA.

<u>AMBA</u>, in *aerobic soils*, reached a maximum concentration of approximately 10% of parent dose, but, more typically, less than 2%. In a separate aerobic soil metabolism study with AMBA as the test substance in three soils, AMBA half-lives were 27, 16, and 20 days, averaging 21 $\pm$ 5 days with an upper 90% confidence interval on the mean of 31 days. In the *anaerobic aquatic* metabolism study discussed above for mesotrione (study conditions were actually "suboxic" rather than anoxic, according to redox and pH measurements) in which parent had a half-life of around 3 to 6 days, AMBA was the only identified *major product*. In this study, AMBA comprised a reviewer estimated maximum of approximately 60% of the total system dose (water plus soil). The kinetic or transformation rate pattern cannot be reliably established for AMBA because of data variability combined with too few sampling time intervals and poor recovery at a critical time point. After a tentative adjustment for recovery, a crude, reviewer-estimated first-order half-life for AMBA (based on data for the final two time points at 30 and 59 days) is 110 days. However, if there is concern for AMBA toxicity at measured maximum concentrations, its persistence under suboxic or anoxic

conditions is best considered undetermined at this time. Thus, in cases where MNBA production in aerobic soil is high and/or early leaching occurs, there would be increased opportunity for production of AMBA at concentrations from roughly a few percent up to roughly 60% of parent dose from a single application.

Carbon dioxide eventually reached major fractions of the mesotrione dose by the end of all studies except hydrolysis and anaerobic (suboxic) metabolism. With the noted exceptions, it was otherwise a ubiquitous product which issued from key positions in both rings of the mesotrione molecule. The cyclohexanedione ring was much more reactive in yielding carbon dioxide than the benzene ring. Evolution of increasing amounts of carbon dioxide from both rings of mesotrione under aerobic conditions (up to about 80% of the dose in some cases after about six months) and increasingly difficult to extract soil residues (tending to increase with time up to roughly15 to 50% of the dose, and then tending to decrease in roughly complementary fashion with increasing levels of carbon dioxide) indicates progression to ultimate degradation/mineralization when there is sufficient aeration. However, when aeration was limited (suboxic conditions), carbon dioxide was only sparingly evolved from either ring. Under such conditions, as stated above, AMBA was a prominent metabolite which may be persistent when oxygen is in short supply.

Mobility/Transport

In Air. Judging from their relatively low Henry's Law constants given in the previous Tables I and II (relatively low vapor pressures coupled with relatively high solubilities in water)[3], volatilization of mesotrione, MNBA, and AMBA is not expected. Consistent with this expectation, in laboratory environmental fate studies there were no appreciable quantities of volatile or gaseous products, except for carbon dioxide.

In Soil and Water (see also Appendix B). There were three separate laboratory batch-equilibrium sorption submissions for parent mesotrione involving 20 different soils. Results for 17 soils were already discussed, tabulated, and given graphically in a previous section above. Simple and Freundlich soil sorption coefficients ranged from approximately 0.18 to 5.0 mL/g. Freundlich sorption coefficients (available for approximately seven soils) were close to the simple coefficients, with 1/n exponents greater than 0.9. Depending strongly on pH, simple, "apparent" Koc values for mesotrione ranged from approximately 15 to 400 mL/g of organic carbon, showing that there is no simple correlation with organic matter alone. However, the demonstrated, remarkable correlation between apparent Koc and pH shows that both soil pH and organic matter govern principally the sorption process for mesotrione.

[3] Henry's Law constants given in Tables I and II are for *unbuffered* water. Since these are distinctly acidic compounds, at typical environmental pHs their solubilities are much higher (as indicated in the tables). Therefore, Henry's Law constants would be inversely much lower still, and corresponding vapor phase partitioning into the atmosphere virtually nil.

There was a separate batch equilibrium submission for each of the transformation products MNBA and AMBA, each in the same five soils; these same five soils were among the twenty mentioned above which were tested with parent mesotrione. *Mesotrione, MNBA, and AMBA may all be characterized simply as highly mobile.* [This mobility is also consistent with their polar, acidic molecular nature and the product label for mesotrione (ZA1296 4-SC) which says that the product is absorbed through the soil by emerging weeds and through the foliage of emerged weeds.] Mesotrione and AMBA were nearly the same in their low affinity for soil. MNBA had even lower, practically immeasurable sorption, and would be essentially unretained by most soils. More specific results for MNBA and AMBA are as follows:

Sorption of MNBA to three of five test soils was essentially negligible within method limits, and at the method "borderline" for the other two. Measured borderline adsorption values (Freundlich Kads) were 0.05 mL/g and 0.16 mL/g (1/n exponents significantly less than one), with corresponding values normalized for organic carbon (Koc) of about 3 and 6 mL/g of organic carbon. Because of the acidic nature of MNBA, sorption is also likely to be affected by pH in a manner similar to parent. However, because of the low sorption, additional refinement of sorption with pH is, for our purposes, the equivalent of splitting hairs.

For AMBA, the five Freundlich K_{ads} values were 0.71 for a silt loam soil, 0.12 for a sandy loam soil, 3.2 for a silty clay loam soil, 0.91 for a clay soil, and 0.18 for a loam soil (1/n exponents between 0.8-0.9); corresponding "apparent" Freundlich K_{oc} values for sorption were approximately 45, 23, 122, 51, and 18 mL/g of organic carbon. Analogous to parent, there was a strong correlation with pH.

Based on their indicated high mobility (low sorption coefficients), if there are human health concerns for exposure to MNBA and/or AMBA, then potential concentrations of these compounds should be considered in a drinking water exposure assessment. Interim results of a prospective groundwater monitoring study in Michigan (see below) are not clear on whether there was actual analysis for MNBA and AMBA.

Terrestrial Field Dissipation (see also Appendix B)

Three terrestrial field dissipation studies on bare ground did not adequately account for the dissipation of mesotrione. The registrant failed to determine dissipation pathways by not identifying any metabolites/degradates in the field or to clearly determine leaching potential. These studies did, however, provide supplemental aspects which are consistent with the laboratory findings of a relatively short residency time for mesotrione in soil. However, short residency times are inconsistent with the long plant-back intervals given on the product label, as given in more detail in the Introduction Section of this document. The registrant should address the apparent inconsistencies.

Prospective Groundwater Monitoring

The registrant has also submitted (without request from the Agency) two interim reports on a prospective groundwater monitoring (PGM) study at a site in Michigan (MRIDs 449017-17, -18). So far, superficial indications are that no leaching of *parent* was occurring. But it is not clear to the reviewer whether there was actually a lab separation step for the transformation products MNBA and/or AMBA, which would be likely candidates for leaching. Although the analytical methods the registrant submitted for water and soil do have provision for 1) chromatographic isolation of each of the three component fractions, parent, MNBA, and AMBA; 2) oxidation of parent fraction to MNBA; and 3) reduction of the MNBA fraction and the oxidized parent fraction to the final common analyte AMBA, it is not clear from the interim reports whether all three fractions were actually isolated and separately analyzed, or whether *only parent fraction* was separated and analyzed after oxidation and reduction. As previously indicated, there is also the question of the adequacy of extraction methodology. The registrant should clarify these uncertainties in the final PGM report. Additionally, soil and groundwater pHs were typically between 7 and 8, where, according to the laboratory data, transformation of mesotrione to metabolites would be more rapid.

Until the registrant submits a final report with study details and actual laboratory sequences for parent *and metabolites* in the PGM study, we cannot project general leaching conclusions. Because of the relatively short environmental residency times for parent, potential leaching concern should be focused on metabolites. Under suboxic or anoxic conditions, as would be associated with ground water, MNBA would be reduced to AMBA. As stated in the metabolite transformation section above, under these conditions the persistence AMBA is incompletely determined. Therefore, we tentatively conclude that either or both of these mobile metabolites may leach to ground water, and that AMBA is likely to be the more prevalent. Hence, as stated previously in the mobility section above, if there are human health concerns for MNBA and/or AMBA exposure, then potential concentrations of these compounds should be considered in any drinking water exposure assessment.

Bioconcentration

Bioconcentration of mesotrione and the identified metabolites MNBA and AMBA is not expected. This expectation is based on low octanol-to-water partitioning ratios (see Tables I and II) which are consistent with the discussed low sorptions to soil organic matter and relatively high solubilities in water for these polar, acidic compounds. On this basis and their relative lack of persistence under aerobic conditions (which decreases opportunity for prolonged surface exposure), the Agency is not requiring any formal study of bioconcentration.

CHAPTER IV

DRINKING WATER ASSESSMENT

The concentrations tabulated below for mesotrione are estimated from first-tier simulation models which use key input parameters derived from data discussed in the Environmental Fate Section above and presented in tables. As discussed, the data show that the environmental fate of mesotrione is correlated with pH, consistent with physicochemical properties and chemical structure. The pH dependence was such that the lower the pH, the higher the soil sorption and the longer the corresponding aerobic soil "half-life" (see previous Table III and Figures 1 and 2). In the particular case of mesotrione, the quantitative correlation between these two factors tends to closely offset or normalize model estimated environmental concentrations to a central value, regardless of pH. The ranges of drinking water concentrations tabulated below are derived from the 17 paired Koc and half-life values for the 17 soils given in Table III. Table III also has a complete listing of estimated environmental concentrations (EEC), key model input factors, and other input assumptions. For screening purposes, we selected the highest values in the rather narrow range of tabulated values. The reasons for choosing the highest values are to 1) insure that our assessment covers an uncertainty associated with certain inefficient chemical extraction procedures, (discussed previously and in more detail in Appendix C) which have a marginal lengthening effect on "half-lives"; and 2) because, within error limits, it is evident that the highest values (in **boldface** type in the tables below) are representative most of the computed values as well as the pHs associated more typically with the intended agricultural use of mesotrione. Estimations are for parent mesotrione only, but collaterally serve to set rough upper bounds on potential MNBA or AMBA concentrations should they present a concern. Based on the data on formation and decline of metabolites in various media, as discussed in the Environmental Fate Section, *for coarse screening purposes, MNBA and/or AMBA concentrations would be expected to be no more than roughly 30 to 40% (50 to 60% in molar equivalents) of those tabulated below for parent mesotrione.* However, because there is a large uncertainty about the persistence of AMBA under anaerobic conditions and perhaps at lower pHs, groundwater concentrations of AMBA could be several times higher than the 30 to 40% estimate.

Drinking Water Screening Concentrations (Tier 1) for Mesotrione

***Surface Water* (estimated from the GENEEC environmental screening model, version 1.2, 5/3/95):**

Acute (Instantaneous) Concentration:	**20 µg/L** (parts per billion or ppb)	
	Range:	10-20 ppb in 17 soils
	Average:	16 ± 3 ppb
	Median:	16 ppb
Chronic (56-Day) Concentration:	**13 µg/L** (parts per billion or ppb)	
	Range:	4-13 ppb in 17 soils
	Average:	8 ± 2 ppb
	Median:	8 ppb

***Ground Water* Results from the SCI-GROW Regression Model (Version 1.0, 11/12/97):**

Acute and Chronic Concentrations:	**0.15 µg/L** (parts per billion or ppb)	
	Range:	0.002-0.15 ppb in 17 soils
	Average:	0.04 ± 0.03 ppb
	Median:	0.03 ppb

CHAPTER V

AQUATIC EXPOSURE AND RISK ASSESSMENT

TOXICITY TO AQUATIC ANIMALS

Many of the studies on the effect of mesotrione on aquatic animals were done under static conditions and nominal concentrations. The percent active ingredient of the technical product was 96.8%. These studies still satisfy the data requirements for acute exposure for the following reasons based on environmental fate data and physicochemical properties:

1. Water solubility was not a limiting factor.

2. Based on adsorption studies, limited sorption of mesotrione and metabolites would not significantly alter test concentrations and, therefore, conclusions.

3. Hydrolysis and photolysis would not be significant under test conditions.

4. Although significant aerobic metabolism would occur, as indicated by aerobic half-lives of a few days to several weeks, the resulting mixture is representative of that to which organisms would be exposed under environmental conditions. Furthermore, separate tests on metabolites indicated toxicities similar to parent.

Acute and Chronic Toxicity to Freshwater Fish

Since the LC_{50} values are greater than 100 ppm, mesotrione is considered practically nontoxic to freshwater fish on an acute basis (MRID 443735-10 and 443735-09).

Data were submitted (MRID 445050-11) for the Freshwater Fish Early Life Stage Study using the Fathead minnow (*Pimephales promelas*). The NOAEC is 11 ppm and the LOAEC is 23 ppm (MATC = 16 ppm), based on a reduction in larval length of fathead minnows exposed to mesotrione. The guideline (72-4a) is fulfilled (MRID 445050-11) for freshwater fish.

Acute and Chronic Toxicity to Freshwater Invertebrates

Mesotrione is categorized as practically nontoxic to freshwater invertebrates. The *Daphnia magna* LC_{50} is 840 ppm ai for the technical grade (MRID 443735-11). The freshwater invertebrate life-cycle study (MRID 445050-10) found an NOAEC of 180 ppm and LOAEC of 300 ppm, based on a survival of daphnids exposed to mesotrione.

Acute and Chronic Toxicity to Estuarine and Marine Fish

Mesotrione is categorized as practically nontoxic to Estuarine fish on an acute basis. The Sheepshead minnow LC_{50} is 410 ppm ai for the technical grade (MRID 445050-07).

Acute Toxicity to Estuarine and Marine Invertebrates

Mesotrione is categorized as slightly toxic to moderately toxic to estuarine invertebrates on an acute basis. The Eastern oyster LC_{50} is 72 ppm ai for the technical grade (MRID 445050-09) and the mysid shrimp LC_{50} is 3.3 ppm (MRID 445050-08).

RISK TO AQUATIC ANIMALS

EFED calculates EECs using the GENeric Expected Environmental Concentration Program (GENEEC). The EECs are used for assessing acute and chronic risks to aquatic organisms. Acute risk assessments are performed using peak EEC values for single and multiple applications. Chronic risk assessments are performed using the 21-day EECs for invertebrates and 56-day EECs for fish.

The EECs selected are tabulated below.

GENEEC Estimated Environmental Concentrations (EECs) for aquatic exposure with the maximum annual application rate (0.43 lb ai/A) applied at one time. Aerial and ground results are essentially the same within error limits. (Likewise, for two split applications at the maximum label rates, risk results for mesotrione do not change significantly.)

Site	Application Method	Application Rate (lbs ai/A)	# of Apps./ Interval Between Applications	Initial (PEAK) EEC (ppb)	21-day average EEC (ppb)	56-day average EEC (ppb)
Corn	aerial application	0.43	2 (14 days)	20	17	13
Corn	ground unincorporated	0.43	2 (14 days)	20	17	13

Risk to Freshwater Fish

The Risk Quotients (RQs) for freshwater fish are based on the worst case assumption that both applications are at once, *i.e.*, at 0.43 lbs ai/A. The initial (peak) EEC was 20 ppb and the 56-day (chronic) EEC was 13 ppb. They were divided by the rainbow trout LC50 of >120 ppm and the fathead minnow MATC of 16 ppm to produce an Acute RQ of <<0.01 and a Chronic RQ of <<0.01. No aquatic acute or chronic levels of concern are exceeded for freshwater fish at any proposed application rate.

Risk to Freshwater Invertebrates

The Risk Quotients (RQs) for freshwater invertebrates are based on the worst case assumption that both applications are applied at once, *i.e.*, at 0.43 lbs ai/A. The initial (peak) EEC was 20 ppb and the 56-day EEC was 13 ppb. They were divided by the daphnid LC50 of 840 ppm and MATC of 230 to produce an Acute RQ of <<0.01 and a Chronic RQ of <<0.01. No aquatic acute or chronic levels of concern are exceeded for freshwater invertebrates at any application rate.

Risk to Estuarine and Marine Animals

Fish - The Risk Quotient (RQ) for estuarine and marine fish is based on the worst case assumption that both applications are applied at once, *i.e.*, at 0.43 lbs ai/A. The initial (peak) EEC was 20 ppb and the 56-day EEC was 13 ppb. They were divided by the sheepshead minnow LC50 of 410 ppm to produce an Acute RQ of <<0.01. No chronic studies have been received. Therefore, a Chronic RQ could not be calculated. The aquatic acute levels of concern was not exceeded for estuarine and marine fish at any proposed application rate.

Invertebrates - The Risk Quotients (RQs) for estuarine and marine invertebrates are based on the worse case assumption that both applications are applied aerially at once, *i.e.*, at 0.43 lbs ai/A. The 21-day EEC was 17 ppb. They were divided by the mysid shrimp LC50 of 3.3 ppm to produce an Acute RQ of <0.01. No chronic study has been received, therefore, no Chronic RQ can be calculated. The aquatic acute level of concern has not been exceeded for estuarine and marine invertebrates at any proposed application rate.

RISK TO NONTARGET AQUATIC PLANTS

Exposure to nontarget aquatic plants may occur through runoff or spray drift from adjacent treated sites or directly from such uses as aquatic weed or mosquito larvae control. An aquatic plant risk assessment for acute high risk is usually made for aquatic vascular plants from the surrogate duckweed *Lemna gibba*. Nonvascular acute high aquatic plant risk assessments are performed using either algae or a diatom, whichever is the most sensitive species. An aquatic plant risk assessment for acute- endangered species is usually made for aquatic vascular plants from the surrogate duckweed *Lemna gibba*. Runoff and drift exposure is computed from GENEEC. The risk quotient is determined by dividing the pesticide's initial or peak concentration in water by the plant EC50 value.

Acute risk quotients for vascular and nonvascular plants are tabulated below.

Acute Risk Quotients for multiple applications to aquatic plants. Toxicities are for duckweed, a vascular plant (*Lemna gibba*) and an alga (*Selenastrum capricornutum* =*Kirchneria subcapitata*). The duckweed EC_{05} was used for the endangered species RQ.

Site/ Application Method/Rate of Application (lbs ai/A)	Species	EC_{05} (ppb)	EC_{50} (ppb)	Initial EEC(ppb)	Endangered Species RQ (EEC/EC_{05})	Nontarget plant RQ (EEC/EC_{50})
Corn/aerial (0.43)	duckweed	7.5	18	20	2.7	1.1
	green alga		1900	20		<0.01

An analysis of the results indicates that endangered species levels of concern for vascular aquatic plants are exceeded for single and multiple application rates; nontarget vascular plant acute levels of concern are exceeded only at the multiple application rate. The nontarget level of concern for algae is never exceeded. There are no endangered algae.

Mesotrione is toxic to vascular aquatic plants but not to nonvascular aquatic plants (algae) at proposed application rates. If mesotrione is added to a body of water inadvertently, by drift or by runoff, it would be expected to reduce the mass of aquatic vascular plant life and the biomass of the animals that depend upon those plants.

CHAPTER VI

TERRESTRIAL EXPOSURE AND RISK

TOXICITY TO TERRESTRIAL ANIMALS

Acute, Sub-Acute, and Chronic Toxicity in Birds

Mesotrione is practically nontoxic to avian species on an acute oral basis. The acute oral LD_{50}fdor the bobwhite quail was >2,000 mg/kg body weight (MRID 443735-06). A subacute dietary study found the Mallard duck's LD_{50} (MRID 443735-08) was >5,130 mg/kg and the Bobwhite quail LD_{50} (MRID 443735-09) was >5,200 mg/kg. Therefore, mesotrione is considered to be practically nontoxic to birds on a subacute dietary basis.

Avian reproduction studies using the TGAI on the preferred species, the mallard duck, found the following results.

Avian Reproductive Toxicity using the TGAI (96.8%) mesotrione.

Species/ Study Duration	NOAEC/ LOAEC (ppm)	LOAEC Endpoints	MRID Author/Year	Study Classification
Mallard duck *(Anas platyrhynchos)*	NOAEC = 120 LOAEC = 600	Normal hatchlings/ eggs laid	445050-05 Johnson, 1997	Core

The results indicate an NOAEC of 120 ppm and an LOAEC of 600 ppm, based on the percentage of normal hatchlings of eggs laid by the mallard.

Acute and Chronic Toxicity to Mammals

Wild mammal toxicity levels were not available. A rat (*Rattus norvegicus*) acute toxicity value (MRID 44373512; Robinson, 1984) was obtained from the Agency's Health Effects Division (HED). The LD_{50} was 5,000 mg/kg based upon the survival of all subjects. A rat reproductive toxicity study (MRID 44920801; Moxon, 1999) found a LOAEL of 2,000 ppm based on ossification. Mesotrione is categorized as practically nontoxic to small mammals on an acute and chronic oral basis.

Toxicity in Insects

A study with 96.8% ai mesotrione (MRID 443735-28) found a 24-hour acute contact LD_{50} greater than 100 µg ai/bee and an oral LD_{50} of 11 µg ai/bee, respectively, which classifies mesotrione as practically nontoxic to bees on an acute basis.

Toxicity in Other Terrestrial Invertebrates

Studies on other terrestrial invertebrates provided supplemental information. The mesotrione LC_{50} for an earthworm *(Eisenia fetida)* was >2,000 mg/kg, > 200 g ai/ha for carabid beetles (*Poecilus cupreus*), and >200 g ai/ha for a parasitic wasp *(Aphidius rhopalosiphi*). The proposed labeled metric rate of application is 200 g ai/ha.

TOXICITY TO TERRESTRIAL PLANTS

For Tier II *seedling emergence*, lettuce is the most sensitive dicot (EC25 and EC05 values are 0.0033 and 0.0012 lb ai/acre, respectively); onion is the most sensitive monocot (EC25 and EC05 values are 0.032 and 0.001 lb ai/acre, respectively). For Tier II *vegetative vigor*, tomato is the most sensitive dicot (EC25 and EC05 values are 0.00023 and 0.0001 lb ai/acre, respectively); onion is the most sensitive monocot (EC25 and EC05 values are 0.0009 and 0.0001 lb ai/acre, respectively) .

EXPOSURE AND RISK TO TERRESTRIAL ANIMALS

The estimated environmental concentrations (EECs) on food items following the application of mesotrione as a liquid are compared to toxicity values to assess risk. The predicted 0-day maximum and mean residues of a pesticide that may be expected to occur on selected avian or mammalian food items immediately following a direct single application are tabulated below. See Appendix E for details of exposure and risk quotient calculations.

Estimated Environmental Concentrations on avian and mammalian food items (ppm) following a single application at 1 lb ai/A.

Food Items	EEC (ppm) Predicted Maximum Residue	EEC (ppm) Predicted Mean Residue
Short grass	240	85
Tall grass	110	36
Broadleaf/forage plants and small insects	135	45
Fruits, pods, seeds, and large insects	15	7

Risk to Birds

For all current maximum application rate scenarios, no avian acute or chronic level of concern is exceeded.

Avian acute and chronic risk quotients are based, respectively, on the mallard duck LC50 of ≥5,130 ppm and mallard duck NOAEC of 120 ppm. For all maximum application rate scenarios for mesotrione (a single preemergence application of 0.16 lb a.i./A, a single postemergence application of 0.27 lb a.i./A, and the combined maximum seasonal rate of 0.43 lb a.i./A), acute risk quotients for broadcast applications of mesotrione are all ≤0.02, well below all levels of concern. Chronic risk quotients are all ≤0.86, which is below the chronic level of concern (1.0).

Risk to Mammals

The mammal RQs are tabulated below.

Acute and chronic risk quotients for wild mammals based on a white rat LC50 of>5,000 ppm and a chronic NOAEL of 2,000 ppm with as single seasonal maximum application rate of 0.43 lbs a.i./A.

Site/App. Method	Food Items	Maximum EEC[1] (ppm)	Acute RQ (EEC/LC50)	Chronic RQ (EEC/NOAEL)
Corn Broadcast	Short grass	103.2	N/A[2]	N/A[2]
	Tall grass	47.3	N/A[2]	N/A[2]
	Broadleaf plants/ Insects	58.1	N/A[2]	N/A[2]
	Seeds	6.45	N/A[2]	N/A[2]

1 Assumes no degradation.
2 The RQ is below 0.01

Even if the maximum seasonal rate is applied at one time, all mammalian acute and chronic RQs are below 0.01. Therefore, no level of concern is exceeded.

Risk to Insects

Currently, EFED does not assess risk to insects. Results of acceptable studies are used for recommending appropriate label precautions.

RISK TO NONTARGET TERRESTRIAL PLANTS

The acute and chronic risk quotients are tabulated below.

Terrestrial plant risk quotients from a single, unincorporated, air application of 0.43 lbs ai/A (the seasonal rate) to a corn field for terrestrial plants in dry and semi-aquatic areas.

Exposure / Plant Type	Seedling Emergence RQ		Vegetative Vigor RQ
	Dry Area	Semi-Aquatic Area	Both Areas
Acute monocot	1.1	4.7	24
Acute dicot	10	46	107
Acute endangered monocot	34	150	215
Acute endangered dicot	29	125	215

An analysis of the results indicates that for a broadcast application of mesotrione at the seasonal maximum application rate, acute endangered species levels of concern (1) and the acute levels of concern (1) are exceeded for monocots and dicots in dry and semi-aquatic areas using the seedling emergence and vegetative vigor toxicity data.

These results show that mesotrione is toxic to terrestrial plants. Therefore, mesotrione could kill nontarget, terrestrial plants when misapplication, drift, or runoff brings it to field borders and into adjacent fields.

This loss of plants could thin the ground cover and reduce the supply of food and cover for animals. This loss could effect the population size of vertebrates and invertebrates.

APPENDIX A
ECOLOGICAL EFFECTS AND ENVIRONMENTAL FATE DATA REQUIREMENTS

Mesotrione   Chemical Number: 122990

GUIDE-LINE	DATA REQUIREMENT	ARE DATA REQUIREMENTS SATISFIED?	MRID	STATUS
71-1(A)	Acute Avian Oral Quail or Duck	YES	443735-06	C
71-2(a)	Avian Dietary/Quail	YES	443735-07	C
71-2(b)	Avian Dietary/Duck	YES	443735-08	C
71-3	Wild Mammals Toxicity- Acute	YES	44373512	C
83-3(a)	Mammalian Developmental Toxicity	YES	44920801	C
71-4(a)	Avian Reproductive/Quail	YES	445050-05	C
71-4(b)	Avian Reproductive/Duck	YES	445050-06	C
72-1(a)	Fish Toxicity Bluegill	YES	443735-09	C
72-1(c)	Fish Toxicity Rainbow Trout	YES	443735-10	C
72-1(c)	Fish Toxicity Rainbow Trout/degradate- MNBA	YES	449012-03	
72-1(c)	Fish Toxicity Rainbow Trout/degradate- AMBA	YES	4499017-02	C
72-2(a)	Invertebrate Toxicity	YES	443735-11	C
72-2(a)	Invertebrate Toxicity/degradate- MNBA	YES	449017-05	C
72-2(a)	Invertebrate Toxicity/degradate- AMBA	YES	449017-04	
72-3(a)	Estuarine/Marine Toxicity Fish	YES	445050-07	C
72-3(b)	Estuarine/Marine Toxicity Mollusk	YES	445050-09	C
72-3(c)	Estuarine/Marine Toxicity Shrimp	YES	445050-08	C
72-4(a)	Early Life Stage Fish	YES	445050-11	C
72-4(b)	Life Cycle Aquatic Invertebrate	YES	445050-10	C
123-1(a)	Seed Germ/Seedling Emergence	YES	445051-19	C
123-1(a)	Seed Germ/Seedling Emergence- adjuvants	NO		
123-1(b)	Vegetative Vigor	YES	445051-19	C
123-1(b)	Vegetative Vigor- adjuvants	NO		
123-2	Aquatic Plant Growth- Tier II	YES	445051-20, -21, -22, -23, & -24	C
141-1	Honey Bee Acute Contact	YES	443735-28	C

APPENDIX A (continued)

STATUS OF ENVIRONMENTAL FATE DATA REQUIREMENTS FOR
MESOTRIONE
EPA Chemical No: 122990
CAS No.: 104206-82-8

Data Requirement	Use Pattern[1]	Does EPA Have Data To Satisfy This Requirement? (yes, no, partially, etc.)	MRID	Must Additional Data Be Submitted Under FIFRA 3(c)(2)(B)?
§158.290 ENVIRONMENTAL FATE				
Degradation Studies-Lab:				
161-1 Hydrolysis	1	yes	44373529	no
161-2 Photodegradation In Water	1	yes	44537108	no
161-3 Photodegradation On Soil	1	supplemental (upgradable)	44505128 & 45196005 (addendum)	no
Metabolism Studies-Lab:				
162-1 Aerobic Soil	1	partially	44373530, (44373531& 45196006), 44505129, 44505208, (44901714, AMBA)	no
162-2 Anaerobic Soil	1	no		no
162-3 Anaerobic Aquatic	1	partially	(44505131 & 44505132, two radiolabels)	no
162-4 Aerobic Aquatic	1	partially	45196011	no
Mobility Studies:				
163-1 Leaching-Adsorption/Desorption	1	yes	44505203, 44505204, 44373532, 44505201 (MNBA) 44505202 (AMBA)	no
Dissipation Studies-Field:				
164-1 Soil	1	supplemental	(44505207 & 44505125), 44505206, (44505205 & 44505126)	no
Accumulation Studies:				
165-4 In Fish	1	no		no
Ground Water Monitoring Studies:				
166-1 Small-Scale Prospective	1	interim reports	44901718, 44901717	other and final reports pending
§158.440 SPRAY DRIFT				
201-1 Droplet Size Spectrum	1	spray drift task force		spray drift task force
202-1 Drift Field Evaluation	1	spray drift task force		spray drift task force

FOOTNOTES: 1. 1=Terrestrial Food; 2=Terrestrial Feed; 3=Terrestrial Non-Food; 4=Aquatic Food; 5=Aquatic Non-Food(Outdoor);6=Aquatic Non-Food (Industrial);7=Aquatic Non-Food (Residential);8=Greenhouse Food; 9=Greenhouse Non-Food;10= Forestry; 11=Residential Outdoor; 12=Indoor Food; 13=Indoor Non-Food; 14=Indoor Medicinal;15=Indoor Residential.

APPENDIX B

Additional Description and Considerations for Selected Environmental Fate Study Results by Guideline Category

Preface. More study specific information which both complements and supplements that given in integrated fashion in the main text of this document follows below; some of the information is necessarily repetitive. Greater technical detail on individual study submissions is given in Data Evaluation Reports (DERs) available from our files. However, as footnoted in the main text, since these studies require interpretation in the special context given in the fate and drinking water assessments, reference to these should be unnecessary except for very specific procedural details. Furthermore, as also footnoted in the main text, the reader or future fate reviewers are cautioned that, because of specific study shortcomings, their partial nature, the existence of several closely related series of studies, and the pH dependence of mesotrione and degradates, individual DERs cannot be used in isolation, but must be taken in the context of all submitted data.

Rather than discussing degradates/metabolites as separate components of the individual studies below, it is logical and convenient to integrate this information into the separate section titled Transformation Products. A discussion of the results of a separate aerobic soil metabolism study for AMBA is also given in that section.

Aerobic Soil Metabolism of Mesotrione. We have systematic and definitive laboratory aerobic soil metabolism data for parent mesotrione in 17 diverse soils (15 U.S. soils, including 13 in one study, and two European soils). As stated and illustrated by table and figures in the main text of this document, aerobic soil half-lives ranged from roughly 4 or 5 days to 30 days, with the variation in half-life, in large part, attributed to pH. Because of certain limitations among various chemical extraction procedures, these half-lives and those from other different studies could be adjusted modestly upwards (in many or most cases) by a variable, subjective estimate of perhaps 10 to 20%. However, within reasonable limits, based on the way we have used the data to characterize the environmental risk from mesotrione, it is not necessary (and may not be possible) to attempt complex, formal, study-by-study adjustments. At agricultural pHs preferred for growing corn (nearer to neutral pHs), shorter soil half-lives tend to occur. Most of the soils tested had lower pH than is desirable for corn agriculture, and these less representative soils trended towards the longer half-lives.

Aerobic aquatic metabolism. Laboratory data for mesotrione are limited to two British natural water-sediment systems: one had an experimental pH of approximately 7.9 and a system half-life (water + sediment) of approximately 4 days; the other had a pH of approximately 6.9 and a system half-life of approximately 6 days. The 95% confidence interval for these half-lives is around 3-11 days. However, because these experimental pHs are higher than those of most of the many soils used in the aerobic soil metabolism studies discussed above, we might expect similarly longer half-lives at lower aquatic system pHs.

Anaerobic aquatic metabolism. Laboratory data for mesotrione are limited to one flooded Radford U.S. soil system (two radiolabels). The intended anaerobic conditions were actually suboxic to moderately reducing, and the flooded aquatic pH was approximately 6.9 to 7. Under this combination of experimental conditions, the half-life average of two radiolabels was approximately 4 days with a 95% confidence interval of around 3-6 days. This anaerobic aquatic half-life compares with an aerobic soil metabolism half-life in the same Radford soil (pH 6.1 to 6.2) of 12-14 days. Since anaerobic processes are typically slower than aerobic, the shorter half-life is somewhat unexpected. The higher aquatic pH and incompletely attained reductive conditions can account for these results which are possibly not representative of more anaerobic conditions. In fact, the results here are essentially the same as those from the two different aerobic aquatic systems discussed above. These results indicate that metabolism progresses under suboxic conditions, and may be more influenced by pH than lower oxygen content.

Photolysis in water. This process for mesotrione was slower than metabolism, as indicated by a laboratory half-life of approximately 80 to 90 sunlight equivalent days. In practical terms and as used in simulation modeling, such a half-life is effectively lengthened under normal environmental conditions to the extent that mesotrione may be regarded as essentially stable to photolysis in water.

Photolysis on soil. These data have a large uncertainty, and may be complicated in part by the occurrence of alternative metabolic processes. Whether included or not, soil photolysis is inconsequential to the present assessment. Superficially, the first-order regression half-life was around 30 days with a 95% confidence interval of approximately 10 to 50 days. Partly because of the uncertainty and because soil photolysis typically has greatly diminished efficacy in the field, it was not factored into the exposure and risk assessment.

Terrestrial field dissipation. Studies on bare ground in North Carolina, Mississippi, and Illinois did not adequately account for the dissipation of mesotrione. They did, however, provide *supplemental* aspects which are consistent with the laboratory findings of a relatively short residency time for mesotrione in soil.

Although parent mesotrione "disappeared" fairly rapidly in these field studies ("disappearance" "half-lives" of 2, 14 and 9 days), 1) no degradates, including MNBA and AMBA which were found in laboratory studies (see Transformation Products below), were detected at any sampling interval; and 2) mesotrione was not observed to leach, as might be expected from lab results (see below). Furthermore, because there was no water balance during the study (or even pan evaporation data), it could not be determined 1) if and when conditions were favorable for leaching (or runoff/horizontal flow), or 2) whether amounts of parent or degradates could have escaped detection by leaching below the maximum depth sampled during the time between sampling intervals and/or by insufficiently low detection limits in the sampled soil profile. Therefore, the "disappearance" "half-lives" cannot necessarily be interpreted as degradative in nature, and it is uncertain if leaching (or runoff) occurred.

Because of the cited fundamental problems and other technical reasons, this study did not meet Subdivision N Guidelines. Thus, these studies presented an unresolved account of the terrestrial field dissipation of mesotrione. However, in spite of the shortcomings, taking the environmental fate and ecotoxicological studies as a whole, and considering the manner in which we have characterized the risk, there would be little value added to satisfactory performance of more conclusive dissipation studies. Therefore, the Agency is not requiring additional terrestrial field dissipation studies at this time.

Transformation Products. Among numerous individually separated products in laboratory metabolism and degradation studies, most constituted less than approximately 2% of the parent dose at any time. Only three compounds, MNBA, AMBA (see attached structures) and carbon dioxide were identified as major by-products. Neither MNBA nor AMBA was persistent under aerobic conditions (see below). Recalcitrant or "unextracted" soil/sediment residues also comprised a relatively large fraction of final products. While AMBA was almost always a minor metabolite in aerobic soil, it was a major product under limited oxygen supply. Data are insufficient to determine with any confidence whether AMBA is persistent under conditions of decreased oxygen concentration.

MNBA, is a **m**ethyl**n**itrosulfonyl**b**enzoic **a**cid (in the acronym, the sulfonyl is "silent"). It was produced in most studies, and was almost always a transient metabolite. Chemical evidence indicates it is the initial benzene ring product which remains after the cyclohexane ring portion of the mesotrione molecule splits away by an oxidative process. MNBA generally reached no more than 10-12% of the parent dose (typically 4 or 5%) in the soils tested, most of which were acidic; however, in three of seventeen aerobic soils with more neutral pHs (more desirable for growing corn), maximum concentrations reached approximately 30, 50, and 60% of the dose. These data suggest that MNBA would be a major product in many soils in which corn is grown. Half-lives for MNBA can only be crudely estimated and are highly uncertain. This is primarily because of low, variable yields or insufficient duration of studies with parent. There were no degradation or metabolism studies conducted separately for MNBA. Highly uncertain "half-lives" for MNBA might range typically from around one to a few days, but, irrespective of kinetics, residual amounts of 1-2% remained at the end of most studies. In at least two soils, MNBA "half-lives" appeared to be measured in one to several months.

AMBA is the amine product formed by reduction of the MNBA nitro group. Maximum concentrations in studies with parent were measured in four aerobic soils, but only estimated indirectly in 13 soils where AMBA was not a reference substance. Concentrations ranged from typically less than 2% up to approximately 10% of parent dose. In a separate aerobic soil metabolism study with AMBA as the test substance in three soils, AMBA half-lives were 27, 16, and 20 days, averaging 21 $\pm$ 5 days with an upper 90%

confidence interval on the mean of 31 days. The only product identified from AMBA metabolism was carbon dioxide (14, 43, and 17% at the end of 56 days of study). Polar metabolites varied from 3-15% of the dose. Unextracted soil residues reached maxima of 48, 37, and 60% of the dose after approximately. 28-56 days. There was no attempt to trap organic volatiles.

In the anaerobic aquatic metabolism study with mesotrione discussed above (which was actually under "suboxic" conditions rather than anoxic, according to redox and pH conditions) in which parent had a half-life of around 3 to 6 days, AMBA was the only identified major product which comprised up to a maximum of approximately 60% of the total system dose (water plus soil). The kinetic or transformation rate pattern cannot be reliably established because of data variability combined with too few sampling time intervals. Therefore, the persistence of AMBA under suboxic or anoxic conditions remains undetermined.

Carbon dioxide eventually reached major fractions of the mesotrione dose by the end of all studies except hydrolysis and anaerobic (suboxic) metabolism. It was otherwise a ubiquitous product which issued from key positions in both rings of the mesotrione molecule. The cyclohexanedione ring was much more reactive in yielding carbon dioxide than the benzene ring. Evolution of increasing amounts of carbon dioxide from both rings of mesotrione under aerobic conditions (up to about 80% of the dose in some cases after about six months) and recalcitrant soil residues (tending to increase with time up to roughly15 to 50% of the dose, and then tending to decrease in roughly complementary fashion with increasing levels of carbon dioxide) indicates progression to ultimate degradation/mineralization.

Sorption to Soil. There are three separate batch-equilibrium sorption submissions for parent mesotrione involving 20 different soils. There is a separate batch equilibrium submission for each of the transformation products MNBA and AMBA, each in the same five soils; these same five soils were among the twenty which were tested with parent mesotrione. Mesotrione, MNBA, and AMBA may be simply characterized as potentially highly mobile. Mesotrione and AMBA were nearly the same in their low affinity for soil, while MNBA was relatively lower still.

Sorption of parent mesotrione in all 20 soils (16 U.S., 2 British, and 2 French) was low (or, inversely, mobility was high). As discussed, tabulated, and plotted in the main text of this document, "apparent" Koc values varied in a pH dependent manner from around 15 to 400 mL/g of organic carbon. In some cases, low sorption taxed method limitations. These sorption values are consistent with relatively low octanol to water partitioning ratios and relatively high water solubilities (see physicochemical properties in main text). Because of some possible instability of parent compound (even though soils were sterilized), ostensible results for parent actually may be for parent plus some transformation products.

Sorption of MNBA to three of five test soils (2 U.S. soils, 3 European) was essentially negligible within method limits and "borderline" for the other two. Measured borderline adsorption values (Freundlich Kads) were 0.05 mL/g for a silt loam soil and 0.16 mL/g for a silty clay loam soil, with corresponding values normalized for organic carbon of about 3 and 6 mL/g of organic carbon. (Freundlich Kd values for the other three soils were simply estimated to be <0.1 mL/g, with upper limit Freundlich Koc values less than 20, 6, and 10 mL/g of organic carbon.) All organic carbon desorption values were measured or estimated to be less than 20 mL/g of organic carbon. Because of the acidic nature of MNBA, sorption is also likely to be affected by pH in a manner similar to parent. However, because of the low sorption limitations, additional refinement of sorption with pH is, for our purposes, the equivalent of splitting hairs. Thus, within method limits, MNBA was essentially unretained by these five soils.

Sorption of AMBA to the same five soils tested with MNBA was also low, but measurably higher than for MNBA. Freundlich Kads values (units of mL/g) were 0.71 for a silt loam soil, 0.12 for a sandy loam soil 3.2, for a silty clay loam soil, 0.91 for a clay soil, and 0.18 for a loam soil; corresponding Freundlich K_{oc} values for sorption were approximately 45, 23, 122, 51, and 18 mL/g of organic carbon. Respective Freundlich desorption values were 1.1, 0.20, 4.1, 2.0, and 0.52 mL/g; corresponding Freundlich Koc for values desorption were 69, 38, 156, 109, and 50 mL/g of organic carbon. There was a strong correlation with pH, analogous to parent.

APPENDIX C

INADEQUACY OF SOIL EXTRACTION METHODS FOR AGED SAMPLES

It is important in all environmental fate studies to determine whether extraction methods efficiently remove available parent compound and related degradates/metabolites from those residues which become irreversibly or truly bound to the soil matrix and unavailable to the biota. In numerous studies for mesotrione, variably high concentrations of unextracted soil residues, ostensibly intractably or permanently bound to soil, prompted the reviewer to compare the different soil extraction procedures used in various studies. Comparison of the soil extraction procedures discussed below indicates that some of them were less successful than others; therefore, these would have an effect on the interpretation of apparent half-lives and availability of parent and/or degradates. ***We conclude from the comparisons given below that the registrant should more fully investigate the effects of sample aging on extraction efficiency, and then standardize soil analytical methodologies accordingly to insure that aged samples containing mesotrione and degradates/metabolites are extracted and separated with reliable quantitative efficiency.***

To the registrant's credit, a large amount of soil analysis data has been submitted as integral parts of many different studies, especially aerobic soil metabolism studies. Combinations and permutations among the various extraction methods used in the various metabolism studies make comparisons possible, but complicated. *In general, the decrease in total soil-retained residues which resulted from more efficient soil extractions was accompanied by a roughly equivalent increase in the percentage of mesotrione recovered.* Aged sorption may have been a factor in variable recoveries. ***Unextracted soil residues began to become problematic after about three days, with the greatest extraction efficiency demonstrated in the aerobic soil metabolism study on thirteen soils, MRID 44505129.***

Generally, comparisons of data from the same soil type among the different aerobic soil metabolism studies indicated that unextracted soil residues were greatest in the studies which employed only one extraction with 0.05M ammonium hydroxide accompanied by subsequent extractions, once with sodium hydroxide, once with ethyl acetate and twice with acetonitrile, MRID 44505208. These comparisons indicate that: (1) an average of around 25% more soil-retained residues and 30% less recovered mesotrione were reported in MRID 44505208 at day 21 than the average reported in the three clay loam soils tested in MRID 44505129 at day 28, (2) around 5% more unextracted soil residues and 6% less recovered mesotrione were reported in MRID 44505208 than was reported for the loam soil from MRID 44505129 at day 28, and (3) around 3 or 4% more unextracted soil residues and 4 or 5% less recovered mesotrione were reported in MRID 44505208 than the average reported for the two sandy loam soils from MRID 44505129 at day 28. *The reviewer notes that the preceding comparisons appear to indicate that the single 0.05M ammonium hydroxide extraction utilized for both the terrestrial field studies (MRID's 44505205, 44505206, 44505207) and the method validation studies (MRID's 44505125, 44505126, 44505127 and*

44505210), even when assisted by additional extraction solvents, may be inadequate to fully extract mesotrione from soils that have been aged three weeks or longer.

The comparison between still another extraction method used in the aerobic soil metabolism study MRID 44505130 resulted in mixed changes for recovery efficiency. Approximately 23% less soil-retained residues and 2 or 3% less recovered mesotrione were reported in MRID 44505130 at day 21 than the average reported for the two silt loam soils from MRID 44505129 at day 28. The results from the harsher methods used in MRID 44505130, with the appearance of two unidentified and previously unreported "artifact" substances, suggest the possibility of decomposition mediated by heating the alkali extraction solvent.

Detailed data from the aerobic soil metabolism study for three soils conducted on the mesotrione metabolite AMBA, MRID 44901714, indicated that acetonitrile demonstrated the greatest extraction efficiency for removal of AMBA from all three soil samples. *However, the reviewer notes that acetonitrile was not employed as an extraction solvent in either the terrestrial field dissipation studies, MRID's 44505205, 44505206 and 44505207, or in the method validation studies, MRID's 44505125, 44505126, 44505127 and 44505210.*

Further confusion was generated by the use of still different extraction methods for the anaerobic aquatic soil metabolism studies conducted on both phenyl- and cyclohexyl-labeled mesotrione, MRID's 44505131 and 44505132, respectively. Based on the totality of these observed results, the reviewer proffers that a survey of different extraction methods/solvents is in order.

The data submitted in the above aerobic soil metabolism studies imply that satisfactory extraction of applied mesotrione with the solvents and techniques investigated in method validation studies, MRID's 44505125, 44505126, 44505127 and 44505210, can be completed efficiently only within the first few days of application. Viewed as a whole, aerobic soil metabolism data demonstrated an increase with time of unextracted soil residues; day 0 ranged from 0 to around 3%, day 7 ranged from around 8 to 24%, and day 21 to day 28 ranged from around 15 to 56%. More specifically, when a comparison between the average unextracted soil residues reported in aerobic soil metabolism study MRID 44505208 (0.2% day 0, 22% day 7, and 49% day 21-28), and the average unextracted soil residues reported in study MRID 44505129 (1.6% day 0, 16.2% day 7, and 31.6% day 28), is examined along side of a comparison between the corresponding average percentage of recovered mesotrione (11.8% day 21-28, MRID 44505208; and 25.4% day 28, MRID 44505129), the emerging trend suggests the possibility that aged sorption may be a factor in detection/extraction efficiency.

In spite of this possibility, soil samples that had been freshly spiked by the addition of a known quantity of mesotrione were utilized as standards for both the terrestrial field dissipation studies, MRID's 44505205, 44505206, 44505207, and for the method validation studies, MRID's 44505125, 44505126, 44505127 and 44505210. The reviewer also finds it interesting that the report dates for all but one of the aerobic soil metabolism studies (MRID 44505130) discussed above, precedes the report dates for three of the method validation studies (MRID's 44505126, 44505127 and 44505210) by at least seven months. Additionally, the report dates for all three of the field dissipation studies precedes the report dates for the same three method validation studies (MRID's 44505126, 44505127 and 44505210) by at least four months. *The reviewer notes that all four of the method validation studies (MRID's 44505125, 44505126, 44505127 and 44505210) may be based on a faulty premise which ignores the effect of aged sorption on soil extraction efficiency.*

APPENDIX D

ECOLOGICAL TOXICITY DATA

TOXICITY TO TERRESTRIAL ANIMALS

Acute and Subacute Toxicity in Birds

One acute oral toxicity study using the technical grade of the active ingredient (TGAI) is required to establish the toxicity of mesotrione to birds. The bobwhite study established an LD_{50} of >2,000 mg/kg body weight. Therefore, mesotrione is considered practically nontoxic to the bobwhite on an acute oral basis. The guideline (71-1) is fulfilled for the bobwhite quail (MRID 443735-06).

Two subacute dietary studies using the TGAI are required to establish the toxicity of mesotrione to birds. The preferred species are mallard duck and bobwhite quail. Results of these studies are tabulated below.

Avian subacute dietary toxicity using mesotrione TGAI (96.8% ai).

Species	5-Day LC_{50} (ppm)	Toxicity Category	MRID Author/Year	Study Classification
Northern bobwhite quail (*Colinus virginianus*)	>5200[1,2]	practically nontoxic	443735-07 Rodgers, 1995	Core
Mallard duck (*Anas platyrhynchos*)	>5130[3]	practically nontoxic	443735-08 Rodgers, 1995	Core

[1] 4770 ppm mean measured concentration
[2] Mortalities (1, 5, and 1 bird(s), respectively) were observed in the 163, 325, and 650 ppm treatment levels and were attributed to pecking by other birds.
[3] No mortality.

Since the LC_{50} values exceed 5,000 ppm, mesotrione is considered practically nontoxic to avian species on a subacute dietary basis. The guideline (71-2) is fulfilled (MRID 443735-07, 443735-08).

Chronic Toxicity in Birds

Avian reproduction studies using the TGAI are required for mesotrione because birds may be subject to repeated or continuous exposure to the pesticide, especially preceding or during the breeding season. The preferred species are mallard duck and bobwhite quail. Results of these studies are tabulated below.

Avian Reproductive Toxicity using the TGAI (96.8%) mesotrione.

Species/ Study Duration	NOAEC/ LOAEC (ppm)	LOAEC Endpoints	MRID Author/Year	Study Classification
Northern bobwhite quail *(Colinus virginianus)* 22 Weeks	NOAEC = 3000 LOAEC = >3000	None were affected	445050-06 Johnson, 1997	Supplemental[1]
Mallard duck *(Anas platyrhynchos)*	NOAEC = 120 LOAEC = 600	Normal hatchlings/eggs laid[2]	445050-05 Johnson, 1997	Core

[1] None of the parameters were affected and the maximum field residue level was not reported.
[2] In addition, the authors reported a significant reduction in the percentage of live 3-week embryos of viable embryos at the 600 and 3000 ppm treatment levels when compared to the control.

The results indicate an NOAEC of 120 ppm and an LOAEC of 600 ppm, based on the percentage of normal hatchlings of eggs laid by the mallard. The guideline (71-4) is fulfilled for the mallard (MRID 445050-05). The guideline (71-4) will be fulfilled for the bobwhite (MRID 445050-06) if the maximum field residue level is 3000 ppm or lower.

Acute and Chronic Toxicity to Mammals

Wild mammal studies are required on a case-by-case basis, depending on the results of lower tier laboratory mammalian studies, intended use pattern and pertinent environmental fate characteristics. In most cases, rat or mouse toxicity values obtained from the Agency's Health Effects Division (HED) substitute for wild mammal studies. These toxicity values are reported below.

Mammalian toxicity.

Species/ Study Duration	% ai	Study Type	Toxicity Value (ppm)	Affected Endpoints	MRID Author, Date
Laboratory rat	96.8	Acute	>5,000 (NOAEL)	Survival	44373512 Robinson, 1984
(*Rattus norvegicus*)	96.8	Develop-mental	2,000 (LOAEL)	Ossification	44920801 Moxon, 1999

An analysis of the results indicates that mesotrione is categorized as practically nontoxic to small mammals on an acute and chronic oral basis.

Toxicity in Insects

A honey bee *(Apis mellifera)* acute contact study using the TGAI is required for mesotrione because its use will result in honey bee exposure. A study with 96.8% ai mesotrione was done. An acute contact study had one mortality out of 30 at a dose of 20 µg/bee and an acute oral study had one mortality out of 30 at 11 µg/bee.

The results classify mesotrione as practically nontoxic to bees on an acute contact basis. The guideline (141-1) is fulfilled (MRID 443735-28).

Toxicity in Other Terrestrial Invertebrates

The studies summarized below were not required but were submitted and reviewed.

Toxicity to earthworms, beetles, and wasps.

Species	% ai	Toxicity	MRID Author/Year	Study Classification
Earthworm *(Eisenia fetida)*	96.8	LC50 >2000 mg ai/kg	445050-12 Bembridge 1996	Supplemental[1]
Carabid beetle *(Poecilus cupreus)*	9.4 (w/w)	LC50 >200 g ai/ha[2]	445050-13 Gill, 1997	Supplemental[1]
Parasitic wasp *(Aphidius rhopalosiphi)*	9.4 (w/w)	LC50 >200 g ai/ha[2]	445050-14 Austin, 1997	Supplemental[1]

[1] Not a guideline requirement
[2] The proposed labeled rate

These studies are not guideline requirements but provide supplemental information on the toxicity of mesotrione to earthworms, beetles, and wasps.

TOXICITY TO FRESHWATER AQUATIC ANIMALS

Acute Toxicity to Freshwater Fish

Two freshwater fish toxicity studies using the TGAI are required to establish the toxicity of mesotrione to fish. The preferred study species is rainbow trout (a coldwater fish) and bluegill sunfish (a warmwater fish). Results of these studies are tabulated below.

Acute freshwater fish toxicity with technical grade mesotrione (95.1% ai).

Species/Study Conditions	96-Hour LC_{50} (ppm)	Toxic Category	MRID Author/Year	Study Classification
Rainbow trout *(Onchorynchus mykiss)*/ static	>120 measured[1]	practically nontoxic	443735-10 Kelso, 1994	Core
Bluegill sunfish *(Lepomis macrochirus)*/ static	>130 measured[1]	practically nontoxic	443735-09 Kelso, 1994	Core

[1]The only concentration used

Since the LC_{50} values are greater than 100 ppm, mesotrione is considered practically nontoxic to freshwater fish on an acute basis. The guideline (72-1) is fulfilled (MRID 443735-10 and 443735-09).

Chronic Toxicity to Freshwater Fish

A freshwater fish early life-stage study using the TGAI is required for mesotrione because the end-use product may be applied directly to water or is expected to be transported to water from the intended use site and its use is likely to be continuous or recurrent regardless of toxicity. The preferred study species is rainbow trout. Results of this study are tabulated below.

Freshwater fish early life-stage toxicity under flow-through conditions with technical grade mesotrione (97.6% ai).

Species/ Study Conditions	NOAEC LOAEC (ppm)	MATC (ppm)[1]	Endpoints Affected	MRID Author/Year	Study Classification
Fathead minnow *(Pimephales promelas)* flow-through	NOAEC = 11 LOAEC = 23 measured	16	Larval length	445050-11 Shillabeer, 1996	Core

[1] Defined as the geometric mean of the NOAEC and LOAEC.

The results indicate an NOAEC of 11 ppm and an LOAEC of 23 ppm, based on a reduction in larval length of fathead minnows exposed to mesotrione. The guideline (72-4a) is fulfilled (MRID 445050-11) for freshwater fish.

Acute Toxicity to Freshwater Invertebrates

A freshwater aquatic invertebrate toxicity study using the TGAI is required to establish the toxicity of mesotrione to aquatic invertebrates. The preferred study species is *Daphnia magna*. Results of this study are tabulated below.

Freshwater invertebrate acute toxicity using technical grade mesotrione (96.8% ai).

Species/ Study Conditions	48-hour EC_{50} (ppm)	Toxicity Category	MRID Author/Year	Study Classification
Waterflea *(Daphnia magna)*/ static	840 measured	practically nontoxic	443735-11 Gentle, 1995	Core

Since the EC_{50} is greater than 100 ppm, mesotrione is considered practically nontoxic to aquatic invertebrates on an acute basis. The guideline (72-2) is fulfilled (MRID 443735-11).

Chronic Toxicity to Freshwater Invertebrates

A freshwater aquatic invertebrate life-cycle study using the TGAI is required for mesotrione since the end-use product may be applied directly to water or be transported to water from the intended use site and its use is such that its presence in water is likely to be continuous or recurrent regardless of toxicity. The preferred study species is *Daphnia magna*. Results of this study are tabulated below.

Freshwater aquatic invertebrate life-cycle toxicity using technical grade mesotrione (96.8% ai).

Species/Study Conditions	21-day NOAEC/ LOAEC (ppm)	MATC[1] (ppm)	Endpoints Affected	MRID Author/Year	Study Classification
Waterflea *(Daphnia magna)* static renewal	NOAEC = 180 LOAEC = 300 measured	230	survival	445050-10 Morris, 1996	Core

[1] Defined as the geometric mean of the NOAEC and LOAEC.

The results indicate an NOAEC of 180 ppm and an LOAEC of 300 ppm, based on survival of daphnids exposed to mesotrione. The guideline (72-4b) is fulfilled (MRID 445050-10).

TOXICITY TO ESTUARINE AND MARINE ANIMALS

Acute and Chronic Toxicity to Estuarine and Marine Fish

Acute toxicity studying with estuarine/marine fish using the TGAI is required for mesotrione because the end-use product is intended for direct application to the marine/estuarine environment or the active ingredient is expected to reach this environment because of its use in coastal counties. The preferred study species is sheepshead minnow. Results of these studies are tabulated below.

Estuarine/Marine fish acute toxicity using technical grade mesotrione (96.8% ai).

Species Study Conditions	96-Hour LC_{50} (ppm)	Toxicity Category	MRID Author/Year	Study Classification
Sheepshead minnow *(Cyprinodon variegatus)* static	410 measured	practically nontoxic	445050-07 Kent, 1994	Core

Since the LC_{50} exceeds 100 ppm, it is categorized as practically nontoxic to estuarine/ marine fish on an acute basis. The guideline (72-3a) is fulfilled (MRID 445050-07).

Because the acute toxicity on mesotrione to estuarine and marine fish is low and since the chronic toxicity to freshwater fish was low, chronic toxicity studies will not be required for estuarine and marine fish.

Acute and Chronic Toxicity to Estuarine and Marine Invertebrates

Acute toxicity studies with estuarine/marine invertebrates using the TGAI are required for mesotrione because the end-use product is intended for direct application to the marine/estuarine environment or the active ingredient is expected to reach this environment because of its use in coastal counties. The preferred study species are the mysid shrimp and eastern oyster. Results of these studies are tabulated below.

Estuarine/Marine invertebrate acute toxicity using technical grade mesotrione (96.8%).

Species/ Study Conditions	96-hour LC_{50}/EC_{50} (ppm)	Toxicity Category	MRID Author/Year	Study Classification
Eastern oyster *(Crassostrea virginica)*/ static, shell deposition	69 (nominal) 72 (measured)	slightly toxic	445050-09 Kent, 1996	Core
Mysid *(Mysidopsis bahia)*/ static	3.3 (measured)	moderately toxic	445050-08 Kent, 1994	Core

Since the EC_{50} and LC_{50} values are between 1.0 and 100 ppm, mesotrione is considered moderately toxic to slightly toxic to estuarine/marine invertebrates on an acute basis. The guidelines 72-3b and 72-3c are fulfilled (MRID 445050-09 and 445050-08).

Because the acute toxicity on mesotrione to estuarine and marine invertebrates is low and since the chronic toxicity to freshwater invertebrates was low, chronic toxicity studies will not be required for estuarine and marine invertebrates.

TOXICITY TO PLANTS

Toxicity to Terrestrial Plants

Terrestrial plant studies (seedling emergence and vegetative vigor) are required for herbicides that have terrestrial nonresidential outdoor use patterns and that may move off the application site through volatilization (vapor pressure >1.0 x 10^{-5} mm Hg at 25°C) or drift (aerial or irrigation) and/or that may have endangered or threatened plant species associated with the application site.

For seedling emergence and vegetative vigor studies the following plant species and groups should be studied: (1) six species of at least four dicotyledonous families, one species of which is the soybean (*Glycine max*) and the second is a root crop, and (2) four species of at least two monocotyledonous families, one of which is corn (*Zea mays*).

Terrestrial Tier II studies are required for all low dose herbicides (those with the maximum use rate of 0.5 lbs ai/A or less) and any pesticide showing a negative response equal to or greater than 25% in Tier I studies.

Tier II studies measure the response of plants, relative to a control, and five or more study concentrations. Results of Tier II toxicity studies on the technical/TEP material are tabulated below.

Nontarget terrestrial plant seedling emergence toxicity (Tier II)

Species	% ai	EC_{25}/EC_{05} (lbs ai/A) Endpoint Affected	MRID Author/Year	Study Classification
Monocot- Corn	40.7	>0.34/0.34 emergence=length	445051-19 Teixeira, 1997	Core
Monocot- Oat	"	0.071/0.019 shoot length	"	"
Monocot- Onion	"	0.028/0.017 shoot length	"	"
Monocot- Ryegrass	"	0.057/0.032 shoot length	"	"
Dicot- Turnip	"	0.034/0.023 shoot length	"	"
Dicot- Soybean	"	>0.34/0.34 emergence=length	"	"
Dicot- Cabbage	"	0.013/0.012 shoot length	"	"
Dicot- Cucumber	"	0.059/0.019 shoot length	"	"
Dicot- Lettuce	"	0.0033/0.0012 shoot length	"	"
Dicot- Tomato	"	0.023/0.017 shoot length	"	"

The table above shows that for Tier II seedling emergence, lettuce is the most sensitive dicot and onion is the most sensitive monocot.

Nontarget terrestrial plant vegetative vigor toxicity (Tier II).

Species	% ai	EC_{25}/EC_{05} (lbs ai/A) Endpoint Affected	MRID Author/Year	Study Classification
Monocot- Corn	40.7	>0.31/0.31 length, weight	445051-19 Teixeira, 1997	Core
Monocot- Oat	"	0.27/0.16 whole plant dry weight	"	"
Monocot- Onion	"	0.0009/0.0001 phytotoxicity	"	"
Monocot- Ryegrass	"	0.070/0.039 whole plant dry weight	"	"
Dicot- Turnip	"	0.00078/0.00023 phytotoxicity	"	"
Dicot- Soybean	"	0.0036/0.0001 whole plant dry weight	"	"
Dicot- Cabbage	"	0.0033/0.0015 whole plant dry weight	"	"
Dicot- Cucumber	"	0.0051/0.0003 phytotoxicity	"	"
Dicot- Lettuce	"	0.0013/0.0003 whole plant dry weight	"	"
Dicot- Tomato	"	0.00023/0.00010 phytotoxicity	"	"

The table above shows that for Tier II vegetative vigor, tomato is the most sensitive dicot and onion is the most sensitive monocot. The guideline for seedling emergence and vegetative vigor (123-1) is fulfilled (MRID 445051-19).

Toxicity to Aquatic Plants

Aquatic plant studies are required for any herbicide that has outdoor nonresidential terrestrial uses that may move off-site by runoff (solubility >10 ppm in water), by drift (aerial or irrigation), or that is applied directly to aquatic use sites (except residential).

Aquatic Tier II studies are required for all low dose herbicides (those with the maximum use rate of 0.5 lbs ai/A or less) and any pesticide showing a negative response equal to or greater than 50% in Tier I studies. The following species should be studied at Tier II: *Kirchneria subcapitata*, *Lemna gibba*, *Skeletonema costatum*, *Anabaena flos-aquae*, and a freshwater diatom.

Results of Tier II toxicity studies on the technical/TEP material are tabulated below.

Nontarget aquatic plant toxicity (Tier II).

Species	% ai	EC_{50} (ppm)	NOAEC/E C_{05} (ppm)	MRID Author/Year	Study Classification
Vascular Plants					
Duckweed *Lemna gibba*	97.6	0.018 (mean measured)	0.008	445051-23 Smyth, 1996	Core
Nonvascular Plants					
Green algae *Kirchneria subcapitata*	95.1	1.9 (mean measured)	0.82	445051-24 Shillabeer, 1997	Core
Marine diatom *Skeletonema costatum*	97.6	20 (mean measured)	0.5	445051-20 Smyth, 1996	Core
Freshwater diatom *Navicula pelliculosa*	96.8	68 (mean measured)	46	445051-21 Smyth, 1996	Core
Blue-green algae *Anabaena flos-aquae*	96.8	132 (mean measured)	56	445051-22 Smyth, 1996	Core

The Tier II results indicate that *Kirchneria subcapitata* is the most sensitive nonvascular aquatic plant. The guideline (123-2) is fulfilled (MRID 445051-23, 445051-24, 445051-20, 445051-21, and 445051-22).

APPENDIX E

EXPOSURE AND RISK CHARACTERIZATION

Risk characterization integrates the results of the exposure and ecotoxicity data to evaluate the likelihood of adverse ecological effects. The means of this integration is called the quotient method. Risk quotients (RQs) are calculated by dividing exposure estimates by acute and chronic ecotoxicity values.

RQ = EXPOSURE/TOXICITY

RQs are then compared to OPP's levels of concern (LOCs). These LOCs are used by OPP to analyze potential risk to nontarget organisms and the need to consider regulatory action. The criteria indicate that a pesticide that is used as directed has the potential to cause adverse effects on nontarget organisms. LOCs currently address the following risk presumption categories: (1) **acute high** -- potential for acute risk is high; regulatory action may be warranted in addition to restricted use classification, (2) **acute restricted use** -- the potential for acute risk is high, but may be mitigated through restricted use classification, (3) **acute endangered species** - endangered species may be adversely affected, and (4) **chronic risk** - the potential for chronic risk is high regulatory action may be warranted. Currently, EFED does not perform assessments for chronic risk to plants, acute or chronic risks to nontarget insects, or chronic risk from granular/bait formulations to birds or mammals.

The ecotoxicity test values (, measurement endpoints) used in the acute and chronic risk quotients are derived from required studies. Examples of ecotoxicity values derived from short-term laboratory studies that assess acute effects are: (1) LC50 (fish and birds), (2) LD50 (birds and mammals), (3) EC50 (aquatic plants and aquatic invertebrates) and (4) EC25 (terrestrial plants). Examples of toxicity test effect levels derived from the results of long-term laboratory studies that assess chronic effects are: (1) LOAEC (birds, fish, and aquatic invertebrates), (2) NOAEC (birds, fish and aquatic invertebrates), and (3) MATC (fish and aquatic invertebrates). For birds and mammals, the NOAEC generally is used as the ecotoxicity test value in assessing chronic effects, although other values may be used when justified. Generally, the MATC (defined as the geometric mean of the NOAEC and LOAEC) is used as the ecotoxicity test value in assessing chronic effects to fish and aquatic invertebrates. However, the NOAEC is used if the measurement end point is production of offspring or survival.

Risk presumptions and the corresponding RQs and LOCs, are tabulated below.

Risk Presumptions for Terrestrial Animals

Risk Presumption	RQ	LOC
Birds		
Acute High Risk	EEC[1]/LC50 or LD50/sqft[2] or LD50/day[3]	0.5
Acute Restricted Use	EEC/LC50 or LD50/sqft or LD50/day (or LD50 < 50 mg/kg)	0.2
Acute Endangered Species	EEC/LC50 or LD50/sqft or LD50/day	0.1
Chronic Risk	EEC/NOAEC	1
Wild Mammals		
Acute High Risk	EEC/LC50 or LD50/sqft or LD50/day	0.5
Acute Restricted Use	EEC/LC50 or LD50/sqft or LD50/day (or LD50 < 50 mg/kg)	0.2
Acute Endangered Species	EEC/LC50 or LD50/sqft or LD50/day	0.1
Chronic Risk	EEC/NOAEC	1

[1] abbreviation for Estimated Environmental Concentration (ppm) on avian/mammalian food items

[2] mg/ft^2 [3] mg of toxicant consumed/day

Risk Presumptions for Aquatic Animals

Risk Presumption	RQ	LOC
Acute High Risk	EEC[1]/LC50 or EC50	0.5
Acute Restricted Use	EEC/LC50 or EC50	0.1
Acute Endangered Species	EEC/LC50 or EC50	0.05
Chronic Risk	EEC/MATC or NOAEC	1

[1] EEC = (ppm or ppb) in water

Risk Presumptions for Plants

Risk Presumption	RQ	LOC
Terrestrial and Semi-Aquatic Plants		
Acute High Risk	EEC[1]/EC25	1
Acute Endangered Species	EEC/EC05 or NOAEC	1
Aquatic Plants		
Acute High Risk	EEC[2]/EC50	1
Acute Endangered Species	EEC/EC05 or NOAEC	1

[1] EEC = lbs ai/A

[2] EEC = (ppb/ppm) in water

EXPOSURE AND RISK TO TERRESTRIAL ANIMALS

For pesticides applied as a nongranular product (*e.g.*, liquid, dust), the estimated environmental concentrations (EECs) on food items following product application are compared to LC50 values to assess risk. The predicted 0-day maximum and mean residues of a pesticide that may be expected to occur on selected avian or mammalian food items immediately following a direct single application at 1 lb ai/A (based on Hoerger and Kenaga (1972) as modified by Fletcher *et al.* (1994)) are tabulated below. The predicted maximum and mean residues are adjusted to the actual rates.

Estimated Environmental Concentrations on avian and mammalian food items (ppm) following a single application at 1 lb ai/A.

Food Items	EEC (ppm) Predicted Maximum Residue	EEC (ppm) Predicted Mean Residue
Short grass	240	85
Tall grass	110	36
Broadleaf/forage plants and small insects	135	45
Fruits, pods, seeds, and large insects	15	7

Risk to Birds

The acute and chronic risk quotients for broadcast applications of mesotrione are tabulated below.

Avian acute risk quotients for single application of mesotrione based on a mallard duck LC50 of 5,130 ppm.

Application Method Lbs a.i. per Acre	Food Items	Maximum EEC (ppm)	Acute RQ (EEC/LC50)
Preemergence broadcast 0.16	Short grass	38.40	N/A[1]
	Tall grass	17.60	N/A[1]
	Broadleaf plants/Insects	21.60	N/A[1]
	Seeds	2.40	N/A[1]
Postemergence broadcast 0.27	Short grass	64.80	N/A[1]
	Tall grass	29.70	N/A[1]
	Broadleaf plants/Insects	36.50	N/A[1]
	Seeds	4.10	N/A[1]

1 The RQ would be well below 0.02.

An analysis of the results indicates that for a single broadcast application of the maximum seasonal rate of mesotrione, no avian acute level of concern is exceeded.

Acute and chronic risk quotients for an assumed maximum seasonal rate of 0.43 lbs. a.i. per acre based on a bobwhite quail LC50 of >5,130 ppm and mallard duck NOAEC of 120 ppm.

Site/ Application Method	Food Items	Maximum EEC[1] (ppm)	Acute RQ (EEC/LC50)	Chronic RQ (EEC/NOAEC)
Corn Broadcast	Short grass	103.2	N/A[2]	0.86
	Tall grass	47.3	N/A[2]	0.39
	Broadleaf plants/Insects	58.1	N/A[2]	0.48
	Seeds	6.45	N/A[2]	0.05

1 Assumes no degradation.
2 The RQ is below 0.02

An analysis of the results indicates that for two broadcast applications of mesotrione, no avian acute or chronic level of concern is exceeded.

Risk to Mammals

Mammalian acute risk quotients for single application of mesotrione based on a white rat LC50 of 5,000 ppm.

Application Method lbs a.i. per Acre	Food Items	Maximum EEC (ppm)	Acute RQ (EEC/LC50)
Preemergence broadcast 0.16	Short grass	38.40	N/A[1]
	Tall grass	17.60	N/A[1]
	Broadleaf plants/Insects	21.60	N/A[1]
	Seeds	2.40	N/A[1]
Postemergence broadcast 0.25	Short grass	64.80	N/A[1]
	Tall grass	29.70	N/A[1]
	Broadleaf plants/Insects	36.50	N/A[1]
	Seeds	4.10	N/A[1]

1 The RQ is below 0.02.

Acute risk quotients for an assumed maximum seasonal rate of 0.43 lbs. a.i. per acre based on a white rat LC50 of >5,000 ppm.

Site/App. Method	Food Items	Maximum EEC[1] (ppm)	Acute RQ (EEC/LC50)
Corn Broadcast	Short grass	103.2	N/A[2]
	Tall grass	47.3	N/A[2]
	Broadleaf plants/Insects	58.1	N/A[2]
	Seeds	6.45	N/A[2]

1 Assumes no degradation.
2 The RQ is below 0.02

Acute risk quotients for an assumed maximum seasonal rate of 0.43 lbs. a.i. per acre based on a white rat LC50 of >5,000 ppm and a chronic LOAEL of 2,000 ppm.

Site/App. Method	Food Items	Maximum EEC[1] (ppm)	Acute RQ (EEC/LC50)	Chronic RQ (EEC/NOAEL)
Corn Broadcast	Short grass	103.2	N/A[2]	N/A[2]
	Tall grass	47.3	N/A[2]	N/A[2]
	Broadleaf plants/ Insects	58.1	N/A[2]	N/A[2]
	Seeds	6.45	N/A[2]	N/A[2]

1 Assumes no degradation.
2 The RQ is below 0.1

An analysis of the results indicates that for two broadcast applications of mesotrione, no mammalian acute level of concern is exceeded. If the season maximum application is applied at once no acute or chronic levels of control are exceeded.

Risk to Insects

Currently, EFED does not assess risk to insects. Results of acceptable studies are used for recommending appropriate label precautions.

EXPOSURE AND RISK TO AQUATIC ANIMALS

EFED calculates EECs using the GENeric Expected Environmental Concentration Program (GENEEC). The EECs are used for assessing acute and chronic risks to aquatic organisms. Acute risk assessments are performed using peak EEC values for single and multiple applications. Chronic risk assessments are performed using the 21-day EECs for invertebrates and 56-day EECs for fish.

The GENEEC program uses basic environmental fate data and pesticide label application information to estimate of the expected EECs following treatment of ten hectares. The model calculates the concentration (EEC) of a pesticide in a one hectare, two meter deep pond, taking into account the following: (1) adsorption to soil or sediment, (2) soil incorporation, (3) degradation in soil before washoff to a water body, and (4) degradation within the water body. The model also accounts for direct deposition of spray drift into the water body (assumed to be 1% and 5% of the application rate for ground and aerial applications, respectively). (When multiple applications are permitted, the interval between applications is included in the calculations.)

The range of key environmental fate input parameters used in the model for this pesticide and final selection of representative EECs are discussed and tabulated in the Environmental Fate and the Drinking Water Sections of this document. Input parameter ranges in 17 soils were approximately: soil Koc = 15 to 400 mL/g of organic carbon, aerobic soil metabolism half-life = 5 to 32 days, water photolysis half-life = 83 days, and aerobic aquatic metabolism half-life = 10 to 60 days. A sample output of one of 17 GENEEC "runs" is attached as Appendix F. The EECs selected are tabulated below.

GENEEC Estimated Environmental Concentrations (EECs) for aquatic exposure with the maximum annual application rate (0.43 lb ai/A) applied at one time.

Site	Application Method	Application Rate (lbs ai/A)	# of Apps./ Interval Between Applications	Initial (PEAK) EEC (ppb)	21-day average EEC (ppb)	56-day average EEC (ppb)
Corn	aerial application	0.43	2 (not given)	20	17	13
Corn	ground unincorporated	0.43	2 (not given)	20	17	13

Risk to Freshwater Fish

The Risk Quotients (RQs) for freshwater fish are based on the worse case assumption that both applications are applied at once, *i.e.*, 0.43 lbs ai/A. The initial (peak) EEC was 20 ppb and the 56-day (chronic) EEC was 13 ppb. They were divided by the rainbow trout LC50 of >120 ppm and the fathead minnow MATC of 16 ppm to produce an Acute RQ of <0.01 and a Chronic RQ of <0.01. No aquatic acute or chronic levels of concern are exceeded for freshwater fish at any proposed application rate.

Risk to Freshwater Invertebrates

The Risk Quotients (RQs) for freshwater invertebrates are based on the worse case assumption that both applications are applied at once, *i.e.*, 0.43 lbs ai/A. The initial (peak) EEC was 20 ppb and the 56-day EEC was 13 ppb. They were divided by the daphnid LC50 of 840 ppm and MATC of 230 to produce an Acute RQ of <0.01 and a Chronic RQ of <0.01. No aquatic acute or chronic levels of concern are exceeded for freshwater invertebrates at any application rate.

Risk to Estuarine and Marine Animals

The Risk Quotient (RQ) for estuarine and marine animals is based on the worst case assumption that both applications are applied at once, *i.e.*, 0.43 lbs ai/A. The peak EEC is 20 ppb; the 56-day EEC is13 ppb. They were divided by the sheepshead minnow LC50 of

410 ppm to produce an Acute RQ of <<0.01. No MATC has been received. Therefore, a Chronic RQ could not be calculated. The aquatic acute levels of concern was not exceeded for estuarine and marine fish at any proposed application rate.

The Risk Quotients (RQs) for estuarine and marine invertebrate are based on the worse case assumption that both applications are applied at once, *i.e.*, 0.43 lbs ai/A. The 21-day EEC was 15 ppb. They were divided by the mysid shrimp LC50 of >3.3 ppm to produce an Acute RQ of <0.01. No chronic study has been received. Therefore, no Chronic RQ can be calculated. The aquatic acute level of concern has not been exceeded for estuarine and marine invertebrates at any proposed application rate.

RISK TO NONTARGET PLANTS

Dry and semi-aquatic areas

Terrestrial plants inhabiting dry and semi-aquatic areas may be exposed to pesticides from runoff, spray drift or volatilization. Semi-aquatic areas are those low-lying wet areas that may be dry at certain times of the year. EFED's runoff scenario is: (1) based on a pesticide's water solubility and the amount of pesticide present on the soil surface and its top one inch, (2) characterized as "sheet runoff" (from one treated acre to an adjacent acre) for dry areas, (3) characterized as "channelized runoff" (10 treated acres to a distant low-lying acre) for semi-aquatic areas, and (4) uses on runoff a value of 0.05 based on it water solubility of >100 ppm.

EECs are calculated for unincorporated ground application only. Formulas for calculating EECs for dry areas adjacent to treatment sites and EECs for semi-aquatic areas are in an addendum. Risk quotients are tabulated below.

As can be seen from the following two plant tables, RQs far exceed the endangered and nonendangerered levels of concern, except for nonendangered monocots in dry areas. For endangered species (first table below), acute RQs for monocots range from 11 to 219. Comparable to monocots, the endangered species acute RQs for dicots range from 9.5 to 215. For nonendangered species (second table below), acute RQs for monocots range from 0.4 to 24. The nonendangered species RQs for dicots range from 3.5 to 107. Currently, there are no separate criteria for chronic risk to plants. As the RQs indicate, mesotrione has high potential to kill nontarget plants.

Plant Acute Risk Quotients (RQs) based on emergence NOAELs and Vegetative Vigor EC05s: for single, unincorporated applications (preemergence (0.19 lbs a.i./A) and postemergence (0.24 lbs a.i./A) and a seasonal (0.43 lbs a.i./A)). All are terrestrial plants in dry and semi-aquatic areas based on emergence NOAELs: (onion 0.001 lbs a.i./A), (lettuce 0.0012 lbs a.i./A), and Vegetative Vigor EC05s: (onion 0.0001 lbs a.i./A), (tomato 0.0001 lbs a.i./A)

Method and Rate of Application (lbs ai/A)	Drift (lbs ai/A)	Total Loading to Adjacent Area (Sheet Runoff + Drift)	Total Loading to Semi-Aquatic Area (Channelized Runoff + Drift)	Monocot Emergence RQ Dry Area	Dicot Emergence RQ Dry Area	Monocot Emergence RQ Semi-Aquatic Area	Dicot Emergence RQ Semi-Aquatic Area	Monocot Vegetative Vigor RQ Both Areas	Dicot Vegetative Vigor RQ Both Areas
Corn, Single Ground/ 0.19	0.0019	0.0114	0.0969	11	9.5	97	81	19	19
Corn, Single Ground/ 0.24	0.0024	0.0144	0.1224	14	12	122	102	120	120
Corn, seasonal Ground/ 0.43	0.0043	0.0258	0.2193	26	22	219	183	43	43
Corn, Single Aerial/ 0.19	0.0095	0.0152	0.067	15	13	66	56	95	95
Corn, Single Aerial/ 0.24	0.012	0.0192	0.084	19	16	84	70	120	120
Corn, seasonal Aerial/ 0.43	0.0215	0.0344	0.151	34	29	150	125	215	215

Plant Acute Risk Quotients (RQs) based on emergence EC25s and Vegetative Vigor EC25s: for single, unincorporated applications (preemergence (0.19 lbs a.i./A) and postemergence (0.24 lbs a.i./A) and a seasonal (0.43 lbs a.i./A)). All are terrestrial plants in dry and semi-aquatic areas based on emergence EC25s: (onion 0.032 lbs a.i./A), (lettuce 0.0033 lbs a.i./A), and Vegetative Vigor EC25s: (onion 0.0009 lbs a.i./A), (tomato 0.0002 lbs a.i./A)

Method and Rate of Application (lbs ai/A)	Drift (lbs ai/A)	Total Loading to Adjacent Area (Sheet Runoff + Drift)	Total Loading to Semi-Aquatic Area (Channelized Runoff + Drift)	Monocot Emergence RQ Dry Area	Dicot Emergence RQ Dry Area	Monocot Emergence RQ Semi-Aquatic Area	Dicot Emergence RQ Semi-Aquatic Area	Monocot Vegetative Vigor RQ Both Areas	Dicot Vegetative Vigor RQ Both Areas
Corn, Single Ground/ 0.19	0.0019	0.0114	0.0969	0.4	3.5	3.0	29	2.1	9.5
Corn, Single Ground/ 0.24	0.0024	0.0144	0.1224	0.5	4.4	3.8	37	2.7	12
Corn, Seasonal Ground/ 0.43	0.0043	0.0258	0.2193	0.8	7.8	6.9	66	4.8	22
Corn, Single Aerial/ 0.19	0.0095	0.0152	0.67	0.5	4.6	2.1	20	11	47
Corn, Single Aerial/ 0.24	0.012	0.0192	0.084	0.6	5.8	2.6	25	13	60
Corn, Seasonal Aerial/ 0.43	0.215	0.0344	0.151	1.1	10	4.7	46	24	107

Aquatic Areas

Exposure to nontarget aquatic plants may occur through runoff or spray drift from adjacent treated sites or directly from such uses as aquatic weed or mosquito larvae control. An aquatic plant risk assessment for aquatic vascular plants is usually made from the surrogate duckweed *Lemna gibba*. Acute risk assessments for nonvascular aquatic plants are performed using either an alga or a diatom, whichever is the most sensitive. An aquatic plant risk assessment for acute-endangered species is usually made for aquatic vascular plants from the surrogate duckweed *Lemna gibba*. To date, there are no known nonvascular plant species on the endangered species list. Runoff and drift exposure is computed with the GENEEC model. The risk quotient is determined by dividing the pesticide's initial or peak concentration in water by the plant EC50 value.

Acute risk quotients for vascular and nonvascular plants are tabulated below.

Acute risk quotients from a single, unincorporated, ground application of 0.43 lbs ai/A (the seasonal rate) to a corn field for aquatic plants areas with a duckweed EC50 and a nonvascular plant (green algae) EC50.

Species	EC_{50} (ppm)	EEC (ppm)	NOAEC (ppm)	Endangered Species RQ (EEC/NOAEC)	Nontarget plant RQ (EEC/EC_{50})
Duckweed (*Lemna gibba*)	0.018	0.020	0.008	2.7	1.1
Green algae (*Kirchneria subcapitata*)	1.9	0.020	0.82	0.024	0.01

PLANT RISK ADDENDUM

EEC Formulas

Calculating EECs for terrestrial plants inhabiting dry areas adjacent to treatment sites:

Unincorporated ground application:
Runoff = maximum application rate (lbs ai/A) x runoff value
Drift = maximum application rate x 0.01
Total Loading = runoff (lbs ai/acre) + drift (lbs ai/A)

Incorporated ground application:
Runoff = [maximum application rate (lbs ai/A) ÷ minimum incorporation depth (cm.)] x runoff value
Drift = maximum application rate x 0.01
(Note: drift is not calculated if the product is incorporated at the time of application.)
Total Loading = runoff (lbs ai/A) + drift (lbs ai/A)

Aerial, airblast, forced-air, and chemigation applications:
Runoff = maximum application rate (lbs ai/A) x 0.6 (60% application efficiency assumed) x runoff value
Drift = maximum application rate (lbs ai/A) x 0.05
Total Loading = runoff (lbs ai/A) + drift (lbs ai/A)

Calculating EECs for terrestrial plants inhabiting semi-aquatic low-lying areas:

Unincorporated ground application:
Runoff = maximum application rate (lbs ai/A) x runoff value x 10 acres
Drift = maximum application rate x 0.01
Total Loading = runoff (lbs ai/A) + drift (lbs ai/A)

Incorporated ground application:
Runoff = [maximum application rate (lbs ai/A)/minimum incorporation depth (cm)] x runoff value x 10 acres
Drift = maximum application rate x 0.01
(Note: drift is not calculated if the product is incorporated at the time of application.)
Total Loading = runoff (lbs ai/A) + drift (lbs ai/A)

Aerial, airblast, and forced-air applications:
Runoff = maximum application rate (lbs ai/acre) x 0.6 (60% application efficiency assumed) x runoff value x 10 acres
Drift = maximum application rate (lbs ai/A) x 0.05
Total Loading = runoff (lbs ai/A) + drift (lbs ai/A)

APPENDIX F

Sample GENEEC (Version 1.2, 5/3/95) Input/Output Table
for
Soil #14 in TABLE III of the Environmental Fate Assessment

RUN No. 14 FOR Mesotrione INPUT VALUES

RATE (#/AC) ONE(MULT)	APPLICATIONS NO.-INTERVAL	SOIL KOC	SOLUBILITY (PPM)	% SPRAY DRIFT	INCORP DEPTH(IN)
.43(.43)	1 1	37.0	15000.0	5.0	.0

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (POND)	PHOTOLYSIS (POND-EFF)	METABOLIC (POND)	COMBINED (POND)
22.00	2	N/A	83.70-10269.99	44.00	43.81

GENERIC EECs (IN PPB)

PEAK GEEC	AVERAGE 4 DAY GEEC	AVERAGE 21 DAY GEEC	AVERAGE 56 DAY GEEC
20.10	19.63	17.18	13.33