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

MEMORANDUM **April 22, 2009**

Subject: Registration Review – Preliminary Problem Formulation for Ecological Risk, Environmental Fate, and Endangered species Assessments for Malathion (PC Code 057701; DP Barcode D359863)

To: Eric Miederhoff, Chemical Review Manager
Special Review Branch
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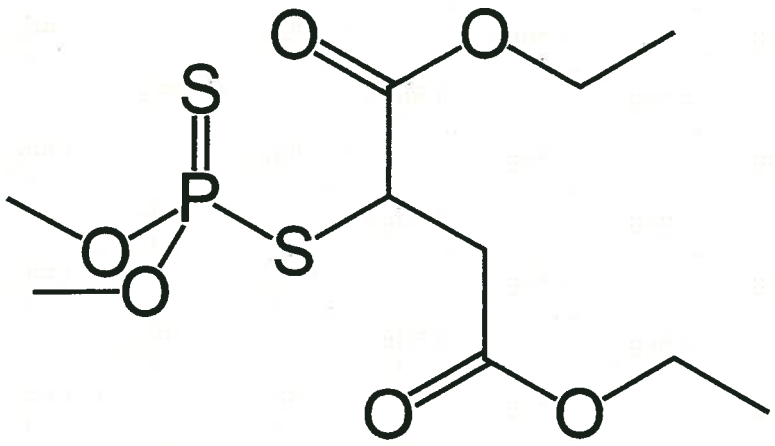
The Environmental Fate and Effects Division (EFED) has completed the preliminary problem formulation (attached) for the ecological risk, environmental fate, and endangered species assessments to be conducted as part of the Registration Review of the organophosphate insecticide, malathion (DP Barcode D359863). The problem formulation draws information from both open literature and studies submitted by the technical registrants in response to data requirements. This document is intended to provide an overview of what is currently known regarding the environmental fate and ecological effects associated with malathion and its degradates and outlines uncertainties regarding attributes of the parent compound and its transformation products. It describes the preliminary ecological risk hypothesis and the processes that will be used during the completion of the ecological risk assessments in support of registration.

Because a drinking water assessment was recently completed (USEPA 2006a supplemented by D292653) using the same application parameters and uses as this problem formulation document, no additional drinking water assessment will be prepared. If application characteristics or uses change, a drinking water assessment may be prepared to assess those changes.

EPA
United States
Environmental Protection
Agency

Office of Prevention, Pesticides,
and Toxic Substances

Problem Formulation for the Environmental Fate, Ecological Risk, and Endangered Species Assessments in Support of the Registration Review of Malathion
Draft: April 22, 2009



Malathion (CAS 121-75-5)

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I. Purpose

The purpose of this problem formulation is to provide an understanding of the environmental fate and ecological effects of the registered uses of malathion. Malathion is a non-systemic organophosphate insecticide and acaricide used to control a wide range of sucking and chewing pests in a variety of field-crops and fruits. Other agricultural uses are protection of stored grain and grasshopper and locust control.

This document will provide a plan for analyzing data relevant to Malathion and for conducting environmental fate, ecological risk, and endangered species assessments for its registered uses. Additionally, this problem formulation is intended to identify data gaps, uncertainties, and potential assumptions used to address those uncertainties relative to characterizing the ecological risks associated with the registered uses of Malathion.

II. Problem Formulation

A. Nature of Regulatory Action

The Food Quality Protection Act of 1996 mandated the EPA to implement a new program for assessing the risks of pesticides, *i.e.*, registration review (http://www.epa.gov/oppsrrd1/registration_review/). All pesticides distributed or sold in the United States generally must be registered by EPA. The decision to register a pesticide is based on the consideration of scientific data and other factors showing that it will not cause unreasonable risks to human health, workers, or the environment when used as directed on product labeling. The registration review program is intended to ensure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health and the environment. Changes in science, public policy, and pesticide use practices will occur over time. Through the new registration review program, the Agency periodically reevaluates pesticides to ensure that as change occurs, products in the marketplace can be used safely.

As part of the implementation of the new Registration Review program pursuant to Section 3(g) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), the Agency is beginning its evaluation to determine whether malathion continues to meet the FIFRA standard for registration. This problem formulation for the environmental fate and ecological risk assessment chapter in support of the registration review is intended for the initial docket opening, which starts the public phase of the review process.

B. Conclusions from Previous Risk Assessments

Malathion has a long regulatory history, and the Agency has conducted numerous ecological risk assessments on this chemical. Several recent ecological risk assessments on malathion serve as a basis for this problem formulation. Each of these are briefly discussed below.

1. Malathion Registration Eligibility Decision, 2006

In 2006, the Agency completed a screening-level ecological risk assessment in support of the Reregistration Eligibility Decision (RED) for malathion (USEPA 2006a). The RED was finalized as part of the organophosphate cumulative assessment (USEPA 2006b). The RED assessment was based on data collected in the laboratory and in the field to characterize the fate and ecotoxicological effects of malathion. Data sources used in this assessment included: 1) registrant submissions in support of reregistration, 2) publicly available literature on ecological effects, 3) monitoring data for freshwater streams, lakes, reservoirs, and estuarine areas, 4) incident reports of adverse effects on aquatic and terrestrial organisms associated with the use of malathion.

The ecological risk assessment in the RED concluded that use of malathion poses a high risk of mortality to fish and aquatic invertebrates from acute toxicity. Almost all uses are expected to pose a high risk of adversely effecting aquatic invertebrate populations, especially in urban streams and wetlands. High acute risk is also expected to fish and amphibians for uses with higher application rates or repeated applications. Numerous incidents of fish kills confirm the acute risk to fish. Use of malathion is generally not expected to pose a high risk of mortality to terrestrial wildlife (birds, mammals, and reptiles, terrestrial stages of amphibians) although the acute level of concern (LOC) is exceeded for some uses with high application rates and repeated applications. Use of malathion poses a risk of impairing reproduction in birds, and may cause other sublethal effects in wildlife. Although no risk assessment was conducted for beneficial insects, the RED concluded that use of malathion poses a hazard to bees and other insect pollinators based on evidence from toxicity studies, field studies, and incidents. Bees may be harmed from direct exposure, exposure to foliar residues, and exposure to residues on pollen brought back to the hive.

The ecological risk assessment in the RED concluded that use of malathion could potential harm all taxa of threatened and endangered animals. Risk quotients exceeded the level of concern for threatened and endangered species of fish, aquatic invertebrates, birds, and mammals.

2. Drinking Water Exposure Assessment, 2006

For the 2006 RED, an assessment was performed of human exposure to malathion and malaoxon (the only degradate of toxicological concern) through consumption of contaminated drinking water (USEPA 2006a). Additional drinking water values were recently supplied to the OPP Health Effects Division (D292653) that better reflect the

application rates, intervals, and number of applications allowed under the Agency's agreement with the registrant and IR-4 (Appendix B).

3. Organophosphate Cumulative Assessment, and Malathion Reregistration Eligibility Decision, 2006

Because the Agency had determined that malathion shares a common mechanism of toxicity with the structurally-related organophosphates insecticides, a cumulative human health risk assessment for the organophosphate pesticides was necessary before the Agency could make a final determination of reregistration eligibility of malathion. This cumulative assessment was finalized in 2006 (USEPA 2006b). The results of the Agency's ecological assessments for malathion are discussed in the July 2006 final Reregistration Eligibility Decision (RED) (USEPA 2006a).

4. California Red-legged Frog Endangered Species Assessment

The Agency also recently completed an endangered species risk assessment of the potential effects of malathion and malaoxon on the threatened California red-legged frog (*Rana aurora draytonii*; CRLF) arising from current uses of malathion (USEPA 2007). Uses included in this 2007 assessment reflected post-RED mitigations. This endangered species risk assessment was part of the *Center for Biological Diversity (CBD) vs. EPA et al.* (Case No. 02-1580-JSW(JL)) settlement entered in the Federal District Court for the Northern District of California on October 20, 2006. The assessment resulted in a determination that the use of pesticide products containing malathion is likely to adversely affect the CRLF. This determination is based on the potential for malathion use to both directly and indirectly affect the species and result in modification to designated critical habitat.

Toxicity values used in this document are in some cases lower than those used in the malathion RED. Although the RED was published in 2006, following completion of the organophosphate cumulative assessment, this ecological risk assessment was compiled in 1999, prior to the regular incorporation of open literature ecotoxicological (ECOTOX) data into EFED risk assessments. Review of the open literature data resulted in a number of lower endpoints. Risk conclusions are similar, in that listed species LOCs are exceeded, but the risk quotients (RQs) presented in this document are higher than corresponding RQs in the RED.

5. Pacific Anadromous Salmonids Endangered Species Assessment

The Agency completed an endangered species risk assessment of the potential effects of malathion on 26 listed Evolutionarily Significant Units (ESUs) of Pacific salmon and steelhead arising from FIFRA regulatory actions regarding use of malathion (USEPA 2004*a*). This risk assessment was part of the *Washington Toxics Coalition vs. EPA* (Case No. C01-132C) order entered in the Federal District Court for the Western District of Washington on July 2, 2002. The assessment concluded that malathion is toxic to fish as well as to organisms that serve as food for threatened and endangered Pacific salmon and

steelhead. The final conclusion was that the uses (at that time) of malathion (and its degradate malaoxon) may affect 24 of these ESUs.

On November 18, 2008, the National Oceanic Atmospheric Administration National Marine Fisheries Service (NMFS) issued a final biological opinion on the effect of pesticide products containing malathion, chlorpyrifos, or diazinon on 28 listed Pacific salmonids (National Marine Fisheries Service, 2008). This opinion concluded that the effects of registration of pesticide products that contain malathion or the two other active ingredients is likely to jeopardize the continued existence of 27 of the 28 species of Pacific salmonids. They concluded that these pesticides are not likely to jeopardize the continued existence of Ozette Lake Sockeye salmon, but may adversely effect that species. Furthermore, they concluded that registration of these products is likely to destroy or adversely modify 25 of the 26 critical habitats that have been designated for these Pacific salmonids. The only critical habitat that they concluded would not be adversely modified is that of the Ozette Lake Sockeye salmon. This Biological Opinion has been included in the docket for this review and is also available on the internet (http://www.nmfs.noaa.gov/pr/pdfs/pesticide_biop.pdf).

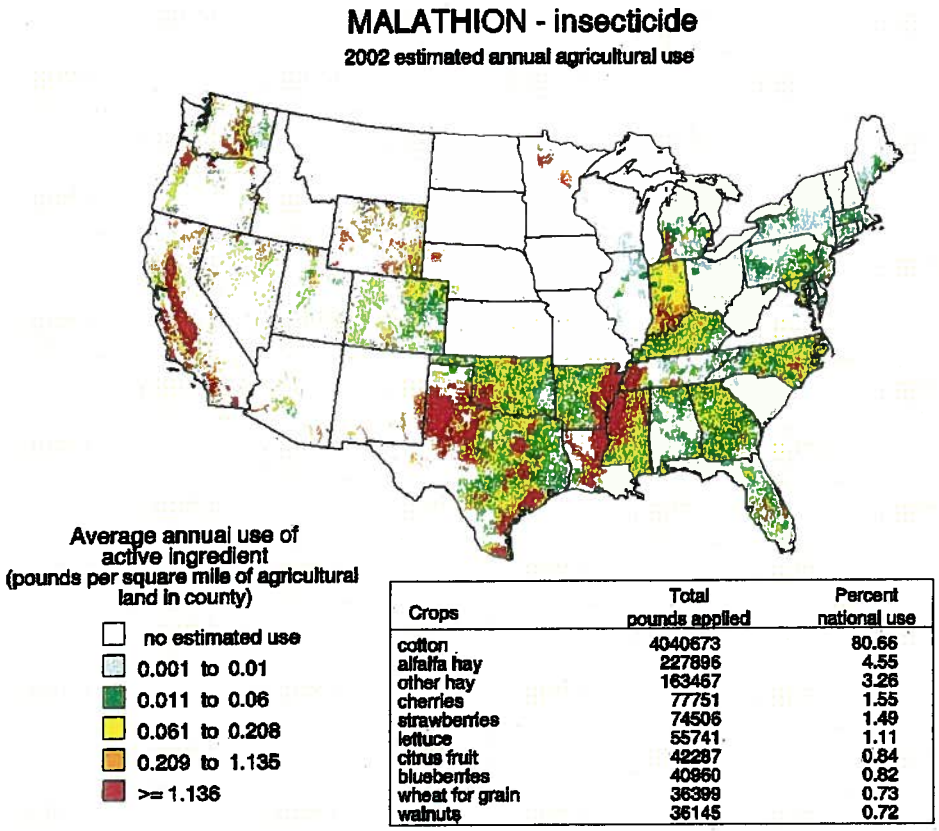
III. Stressor Source and Distribution

A. Mechanism of Action

Malathion, diethyl (dimethoxyphosphinothioylthio)succinate, is a non-systemic insecticide/acaricide belonging to the organophosphate class of pesticides, which acts via contact, ingestion, and respiratory exposure pathways. On a molecular level, the pesticide acts through inhibition of acetylcholinesterase and is used to kill a broad range of insects and mites. Organophosphate toxicity is based on the inhibition of the enzyme acetylcholinesterase which cleaves the neurotransmitter acetylcholine. Inhibition of acetylcholinesterase by organophosphate insecticides, such as malathion, interferes with proper neurotransmission in cholinergic synapses and neuromuscular junctions (USEPA 2006*a*).

B. Overview of Pesticide Usage

Malathion was developed by American Cyanamid in 1952. Cheminova acquired American Cyanamid's malathion business in 1991. (http://www.cheminova.com/en/insecticides/fyfanon/background.htm).
Malathion is one of the most widely used insecticides in the U. S. for residential as well as agricultural pest control. It is used throughout the United States. The predominant agricultural use is on cotton (80% based on 2002 data), but is also applied to a number of other agricultural commodities (Figure 1). It is also used extensively in non-agricultural settings for residential insect control and for adult mosquito control by municipal vector control programs. A list of all labeled uses and their application information (*e.g.*, rate, number, method) is included in Appendix B.



Crops	Total pounds applied	Percent national use
cotton	4040673	80.66
alfalfa hay	227896	4.55
other hay	163457	3.26
cherries	77751	1.55
strawberries	74506	1.49
lettuce	55741	1.11
citrus fruit	42287	0.84
blueberries	40960	0.82
wheat for grain	36399	0.73
walnuts	36145	0.72

Figure 1. Distribution of agricultural applications of malathion in 2002.

Based on an agreement with the Agency, the technical registrant, and the USDA, Inter-regional workgroup #4 (IR-4), all agricultural crops will be limited to the maximum application rates, minimum treatment interval, and maximum number of applications specified in Appendix Table B1. Therefore, EFED's registration review assessment will be based on these agreed rates, application intervals, and number of applications in Appendix B (Eric Miederhoff, Chemical Review Manager, SRRD). However the agreement specifies only maximum number of applications *per season* rather than maximum number of applications *per year*. Therefore for crops that have more than one crop cycle or season per year, the maximum number of applications *per year* will be estimated using conservative assumptions regarding the maximum number of crop cycles per year. (Many of the current labels do not contain sufficient information to limit the maximum annual application rate, minimum treatment interval, and maximum annual number of applications.)

C. Environmental Fate and Transport

Registrant-submitted data defining the physical, chemical, fate, and transport characteristics associated with malathion are summarized in Table 1 and discussed in detail in Appendix A. In past assessments involving malathion, half-life values for water and soil photolysis were extrapolated far beyond the termination on the respective study durations. However, the registrant submitted studies indicate that the photolysis potential for malathion in the environment is limited because the region of the electro-magnetic spectrum in which malathion absorbs is not within the range of natural sun-light. Therefore, malathion is assumed to be stable to photolysis both in water and on soil.

Table 1. General chemical and environmental fate properties of malathion.

Chemical/Fate Parameter	Value(s)	Source (MRID)
Molecular weight (MW) (g/mol)	330.3	Product Chemistry
Vapor pressure (VP) (torr; at 30°C)	4×10^{-5}	Product Chemistry
Water solubility (mg/L; at 25°C)	145	Product Chemistry
Henry's Law Constant (atm-m^3/mol; at 25°C)	1.2×10^{-7}	Calculated[1]
Hydrolysis half-lives (25°C) (days)	107 (pH 5) 6.21 (pH 7) 0.5 (pH 9)	40941201
Water photolysis half-life	Stable	41673001
Soil photolysis half-life	Stable	41695501
Aerobic soil metabolism half-life (days)	3	Malathion CRLF
Organic carbon normalized partition coefficients (K_{OC}) (L/kg_{OC})	151 (Sandy loam) 308 (Sand) 176 (Loam) 183 (Silt loam) 267 (Sandy loam)	41345201
Octanol-water partition coefficient (K_{OW})	613 (Log K_{OW} = 2.79) 628 (Log K_{OW} = 2.80) 560 (Log K_{OW} = 2.748) 2000 (Log K_{OW} = 3.30) 195 (Log K_{OW} = 2.29)	40119201 158054 and 158062 40944103, 40944104, and 40944108 40966603 EPI Suite
Fish bioconcentration	4.2 to 18 × (edible) 37 to 204 × (viscera) 23 to 135 × (whole fish)	43106401, 43106402, and 43340301

[1] Calculated according to USEPA 2002 by: (VP*MW)÷(760*solubility).

Malathion chemically breaks down into many degradate chemicals. Of these identified degradates, only malaoxon was sufficiently toxic to be considered a degradate of concern (approximately 22 times as toxic as malathion in mammals). Chemically, the only difference between malathion and malaoxon is the substitution of oxygen for sulfur at its double bond to phosphorous. Because little fate data is available for malaoxon, aerobic aquatic metabolism, aerobic soil metabolism, hydrolysis, and batch equilibrium data for

malaoxon are requested in this document. (It should be noted that the hydrolysis and aerobic aquatic metabolism studies for malaoxon were also requested in the RED.)

A major problem with the fate data set for malathion is that it is difficult to differentiate between degradation due to hydrolysis and other degradation and dissipation pathways. Hydrolysis half-lives vary by more than 2 orders of magnitude from 12 hrs. (pH 9) to 107 days (pH 5) over a range of only 4 pH units. Because water is present in most of the guideline studies and most of the fate studies were performed under neutral to alkaline conditions, it would be beneficial to have the guideline studies performed under mildly acidic conditions where hydrolysis will have a much more limited effect and therefore, allow the other degradation and dissipation rates to be accurately measured. At this time only aerobic aquatic metabolism and aerobic soil metabolism studies under acidic conditions are requested for malathion.

Other important routes of dissipation from soil suggested by the data include leaching and surface runoff. Malathion and its degradates, in general, are soluble and do not adsorb strongly to soils.

Acceptable leaching data on parent malathion indicate that it is mobile in all soils tested (K_ds of 0.82 - 2.47). Acceptable terrestrial field dissipation data indicate rapid dissipation ($T_{1/2}$ = <2 days). One detection of malathion below 12 inches was found in a terrestrial field dissipation study, indicating leaching as a likely route of dissipation. Similarly, column leaching studies demonstrated that malathion and its degradates, malathion mono- and dicarboxylic acids are very mobile in soil. Data presented to the Agency and in the "Pesticides and Groundwater Database" (USEPA 1992) demonstrate that malathion has the potential to leach to ground water. Malathion has been detected in ground water in three states (California, Mississippi, and Virginia) at levels ranging from 0.03 to 6.17 µg/L. Based on these data and the low K_d values, it is clear that malathion has the potential to leach to ground water.

Although little or no malaoxon production is observed in registrant submitted aquatic studies, malaoxon has been detected in surface waters and the potential for malaoxon runoff may be heightened relative to malathion because it is expected to have higher solubility. EFED is not aware of reports of malaoxon groundwater contamination. However, malathion has contaminated groundwater in several states and has the potential to contaminate surface water through runoff. The increased polarity of malaoxon due to the substitution of oxygen for sulfur increases the expected potential of this chemical to be mobile in soil.

Under many circumstances, malathion degrades rapidly to compounds of lower toxicity (other than malaoxon), probably through microbial metabolism and/or hydrolysis. However, in urban areas (*e.g.*, aerial and ground application for mosquito control), it is likely that malathion will contact dry, microbially inactive, and low organic content surfaces such as concrete, asphalt, dry soil, roofing material, and glass. It is expected that malaoxon production will be increased on these surfaces as malathion is exposed to air for extended periods until it is washed away by rain. This is supported by malaoxon monitoring data in urban streams after malathion treatments to urban areas showing

similar or higher levels of malaoxon than malathion in some instances (CaEPA, 1981). CaEPA has published two studies measuring malaoxon production on dry soil (CaEPA 1993) and steel sheets (CaEPA 1996). Both of these studies showed higher malaoxon production than registrant submitted studies, but maximal levels of malaoxon production were not achieved. On the steel surface a rainfall event removed most of the malathion after only 2 days. On the dry soil malaoxon production did not decrease by the time the study was terminated at 22 days. In a separate but forthcoming DCI (data call in), a study of malaoxon production on dry surfaces will be required.

CaEPA has published a study describing malaoxon production on low organic content soil (0.6%) with a moisture content less than 1% (CaEPA 1993) showing higher malaoxon production than registrant submitted studies using soils with higher organic (2-2.7%) and moisture (75% of water holding capacity, capacity not stated) content. Based on the CaEPA data, it appears that malaoxon production is favored on dry soils and thus may represent a higher risk scenario for malaoxon production and runoff.

The short soil persistence of malathion reduces the risk of leaching to groundwater however it has been detected in the groundwater of at least three states (USEPA 1992). Malaoxon was not detected in any leachate or soil extracts in concentrations ≥0.12% (≥6 µg/L) of applied radioactivity (MRID 43868601, 41345201, 43166301)

Three different malathion formulations [Ready To Use (RTU), Ultra Low Volume (ULV), and Emulsifiable Concentrate (EC)] added to a silt loam soil did not undergo any appreciable volatilization, when measured under different soil moisture regimes or air flow rates. No more than 5.1% of the applied radioactivity volatilized during the 16 days of the study.

A number spray drift studies have been submitted to the Agency by the Spray Drift Task Force. In addition, a study conducted for the Boll Weevil Eradication Program at Pennsylvania State University (1993) examined malathion drift under conditions of boll weevil control (1 lb/A = 112 mg/m^2) with an ultra-low volume (ULV) formulation. Deposition up to 21.0, 11.5, 2.9, and 0.7% of that applied was observed at 100, 200, 500, and 1000 meters downwind, respectively. Due to the size of the particles generated, the ULV formulation is expected to produce the highest levels of drift.

EFED policy is to assume spray drift is equal to 1% of the applied spray volume from ground applications and 5% from aerial and orchard airblast applications at 100 feet downwind for ecological risk assessments. Measured ULV drift data from the Boll Weevil Eradication Program will be considered in the exposure analysis and may be used to evaluate the distance from application sites that potential risks exceed LOCs for ULV applications since the submitted drift studies on ULV malathion show significantly higher levels of drift.

IV. Receptors

Consistent with the process described in the Overview Document (USEPA, 2004*b*), the risk assessment for malathion will rely on a surrogate species approach. Toxicological data generated from surrogate test species, which are intended to be representative of broad taxonomic groups, are used to extrapolate to potential effects on a variety of species (receptors) included under these taxonomic groupings.

Acute and chronic toxicity data from studies submitted by pesticide registrants along with the available open literature are used to evaluate the potential direct and indirect effects of malathion on aquatic and terrestrial receptors. This includes toxicity data on the technical grade active ingredient, degradates, and when available, formulated products (*e.g.* "Six-Pack" studies). The open literature studies are identified using EPA's ECOTOX database (http://cfpub.epa.gov/ecotox/), which employs a literature search engine for locating chemical toxicity data for aquatic life, terrestrial plants, and wildlife. The evaluation of both sources of data can also provide insight into the direct and indirect effects of malathion on biotic communities from loss of species that are sensitive to the chemical and from changes in structure and functional characteristics of the affected communities.

A. Effects to Aquatic Organisms

Table 2 provides a summary of toxicity data for surrogate aquatic species that the EPA plans to use to characterize potential acute and chronic ecological effects of malathion. This table provides only the results of studies that indicate the greatest toxicity for each aquatic taxonomic group for which toxicity data are available. A complete listing of all freshwater ecotoxicology data for malathion known by the Agency is available in the *Risks of Malathion Use to Federally Listed California Red-legged Frog (Rana aurora draytonii)* (USEPA 2007, http://www.epa.gov/espp/litstatus/effects/redleg-frog/malathion/determination.pdf). A complete listing of all saltwater ecotoxicology data for malathion with toxicity endpoints suitable for the Agency's screening risk assessment for aquatic organisms is available in Appendix C.

Table 2. Toxicity results that the Agency plans to use to assess ecological effects of malathion to aquatic species and the associated acute toxicity classification.

Taxonomic Group	Toxicity Type	Surrogate Species	Acute Toxicity – Chronic Toxicity	MRID, Citation	Acute Toxicity Classification
Freshwater fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	96-hr LC_{50} = 4.1 µg/L	40098001 (Mayer and Ellersieck, 1986)	Very highly toxic
	Chronic	Flagfish (*Jordanella floridae*)	NOAEC = 8.6 µg/L LOAEC = 11 µg/L	Hermanutz, 1978	--
Amphibian	Acute	Indian bullfrog, six-fingered frog	96-hr LC_{50} = 0.59 µg/L	ECOTOX Ref. No. 011521	--
Freshwater invertebrates	Acute	Water flea (*Ceriodaphnia dubia*)	24-hr EC_{50} = 0.098 µg/L	ECOTOX Ref. No. 05539 (Rawash et al., 1975)	Very highly toxic

Taxonomic Group	Toxicity Type	Surrogate Species	Acute Toxicity -- Chronic Toxicity	MRID, Citation	Acute Toxicity Classification
	Chronic	Water flea (*Daphnia magna*)	NOAEC = 0.060 µg/L LOAEC = 0.10 µg/L	MRID 41718401 (Blakemore and Burgess, 1990)	--
Estuarine/marine fish	Acute	Sheepshead minnow (*Cyprinodon variegates*)	96-hr LC50 = 33 µg/L	MRID 41174301 (Bowman 1989)	Very highly toxic
		Bluehead (*Thalassoma bifasciatum*)	96-hr LC_{50} = 27 µg/L[1]	ECOTOX Ref. No. 000628 (Eisler, 1970)	Very highly toxic
	Chronic	Red drum (*Sciaenops ocellatus*)	9-d NOAEC = 7.4 µg/L LOAEC not determined[1]	ECOTOX Ref. No. 081672 (Alvarez, 2005)	--
Estuarine/marine invertebrates	Acute	Mysid shrimp (*Americamysis bahia*)	96-hr EC_{50} = 2.2 µg/L	MRID 41474501 (Forbis, 1990)	Very highly toxic
Aquatic plants (nonvascular)	Acute	Green algae (*Pseudokirchneriella subcapitata*)	2-day IC_{50} = 2040 µg/L NOEC = 500 µg/L	ECOTOX Ref. No. 85816	--
Aquatic plants (vascular)	Acute	Large duckweed (*Spirodela polyrhiza*)	NOEC = 24 mg/L	ECOTOX Ref. No. 9184	--

[1] The Agency has not yet reviewed the study methods and results of this study to determine its acceptability. The result presented is tentative pending this review. If found acceptable, this result would be the most sensitive endpoint for estuarine/marine fish.

On an acute exposure basis, technical grade malathion is classified as very highly toxic to all taxonomic groups of aquatic animals, including fish, aquatic-phase amphibians, and aquatic invertebrates. In fish, chronic exposure to malathion results in observable sublethal effects beginning at concentrations between 8.6 and 11 µg ai/L. In invertebrates, observable sublethal effects from chronic exposure occurs at much lower concentrations, between 0.060 and 0.10 µg ai/L. No phytotoxicity data has been submitted to the Agency to assess the toxicity of malathion to plants. Data from the open literature indicate that malathion may be toxic to some nonvascular aquatic plants at concentrations above 500 µg/L and to vascular aquatic plants at concentrations above 24 mg/L.

The registrant submitted additional toxicity data on the acute toxicity of malathion to aquatic organisms in September 2008. These studies, along with the results reported by the study authors, are listed in Table 3. These studies have not yet been reviewed by the Agency. The Agency will review these studies as part of registration review process and determine their acceptance classification. Until they are reviewed, the results are considered preliminary and subject to change. However, based on preliminary results, it appears unlikely that any of these studies will indicate greater toxicity (*i.e.*, yield a lower LC_{50} or EC_{50}) than the study for the corresponding test guideline reported in Table 32. Therefore, the results of these studies are not expected to affect the quantitative conclusions of the assessment of acute risk of malathion to aquatic organisms.

Table 3. Preliminary toxicity results from unreviewed studies on the ecological effects of malathion to aquatic species and the associated acute toxicity classification.

Taxonomic Group	Test Material	% A.I.	Surrogate Species	Acute Toxicity (preliminary estimate)	MRID, Citation
Freshwater fish	Technical malathion	96.9	Rainbow trout (*Oncorhynchus mykiss*)	96-hr LC_{50} = 180 µg/L	47540302 (Gries and Purghart, 2001a)
	Technical malathion	96.9	Bluegill sunfish (*Lepomis mcrochirus*)	96-hr LC_{50} = 54 µg/L	47540304 (Gries and Purghart, 2001b)
	CHA 3110	40.6	Rainbow trout (*Oncorhynchus mykiss*)	96-hr LC_{50} = 300 µg/L[1]	47540304 (Gries and Purghart, 2001c)
Freshwater invertebrates	Technical malathion	96.9	Water flea (*Daphnia magna*)	48-hr EC_{50} = 0.72 µg/L	47540303 (Gries and Purghart, 2001d)

[1] Based on measured concentration of active ingredient.

Based on toxicity information reported in the risk assessment for the California Red-legged Frog (USEPA 2007), the sensitivity of aquatic organisms exposed to a formulated product of malathion is similar to or less than the sensitivity of organisms exposed to technical grade malathion. For example, acute toxicity testing with the waterflea (*Daphnia magna*) measured an EC_{50} of 2.2 µg ai/L (confidence interval 1.9-2.5 µg ai/L) when exposed to TGAI with 95% active ingredient (MRID 41029701), compared to 1.0 µg ai/L (confidence interval 0.7-1.4 µg ai/L) when exposed to Cythion 57% EC. Therefore, the focus of this assessment will be on the TGAI of malathion and its malaoxon degradation product.

B. Effects to Terrestrial Organisms

Table 4 provides a summary of toxicity data for surrogate terrestrial species that the EPA plans to use to characterize potential acute and chronic ecological effects of malathion. This table provides only the results of studies that indicate the greatest toxicity for each terrestrial taxonomic group for which toxicity data are available. A more comprehensive discussion of terrestrial ecotoxicology data for malathion known by the Agency is provided in *Risks of Malathion Use to Federally Listed California Red-legged Frog (Rana aurora draytonii)* (USEPA 2007, http://www.epa.gov/oppfead1/endanger/litstatus/effects/redleg-frog/malathion/determination.pdf).

Table 4. Toxicity results that the Agency plans to use to assess potential ecological effects of malathion to terrestrial species and the associated acute toxicity classification.

Taxonomic Group	Toxicity Type	Surrogate Species	Toxicity	MRID, Citation	Acute Toxicity Classification
Birds[1]	Acute Oral	Ringed-necked pheasant (*Phasianus colchicus*)	LD_{50} = 1.44 mg/kg	001600000 (Hudson et al. 1984)	Moderately Toxic
	Subacute Dietary	Japanese Quail (*Coturnix japonica*)	LC_{50} = 2128 mg/kg-diet	ECOTOX Ref. No. 035214	Slightly Toxic

Taxonomic Group	Toxicity Type	Surrogate Species	Toxicity	MRID, Citation	Acute Toxicity Classification
	Chronic	Northern Bobwhite (*Colinus virginianus*)	NOAEL = 110 mg/kg-diet, LOAEL=350 mg/kg-diet, regressed ovaries and enlarged/flaccid gizzards	435015-01 (Beavers et al, 1995)	--
Mammals	Acute	Laboratory rat (*Rattus norvegicus*)	LD_{50} = 1000 mg/kg	Doc # 000389 (Karlow and Martin, 1965)	Slightly Toxic
	Chronic	Laboratory rat (*Rattus norvegicus*)	NOAEL = 240 mg/kg-diet LOAEL = 1000 mg/kg-diet, reduced pup survival and BW	Doc # 000389 (Karlow and Martin, 1965)	--
Insects	Acute Conact	Honey bee (*Apis mellifera L.*)	8-hr LD_{50} (contact) = 0.20 µ/bee	05004151 (Stevenson 1968)	Very highly toxic
	Residues on foliage	Honey bee (*Apis mellifera L.*)	LD_{50} < 1.6 lb/a	41208001 41284701	--

[1] Birds represent surrogates for terrestrial-phase amphibians and reptiles.

Malathion is classified as moderately toxic to birds, which are used as surrogate species for terrestrial-phase amphibians and reptiles, on an acute oral exposure basis, and as slightly toxic to birds, terrestrial-phase amphibians, and reptiles on a subacute dietary exposure basis, and slightly toxic to mammals. Chronic exposure to malathion results in adverse reproductive effects at dietary concentration between 110 and 350 mg/kg-diet in birds, and between 240 and 1000 mg/kg-diet in mammals.

Acute contact toxicity data submitted to the Agency indicate that malathion is very highly toxic to beneficial insects such as the honeybee. Toxicity data that the Environmental Fate and Effects Division has obtained from the U.S. EPA ECOTOX Database for the honey bee, the alfalfa leafcutter bee, and the alkali bee also places the acute toxicity of malathion in the very highly toxic category. Data on toxicity of residues on foliage indicate that when applied in a formulated product with 57% ai (CYTHION Insecticide 5E) at a rate of 1.6 lb ai/acre, residues on foliage remain toxic to bees for at least 8 hours after treatment. During the Registration Review, the Agency will be reviewing the numerous other laboratory and field studies on the toxicity of malathion to beneficial insects that have been published in the scientific literature. The Agency does not expect a need to request field testing for pollinators (guideline 158.3040) because existing data from submitted bee toxicity studies and from bee studies published in the open literature is sufficient to characterized the hazard of malathion to pollinators.

No phytotoxicity data has been submitted to the Agency to assess the toxicity of malathion to terrestrial plants. Studies reported in the open literature have not shown any phytotoxic effects of malathion that could be associated with adverse to growth and survival of plants under field conditions. Furthermore, phytotoxicity data available for other organophosphate insecticides indicate a general lack of phytotoxicity of pesticides of this class. Therefore, malathion is not expected to have significant toxicity to terrestrial plants at environmentally relevant concentrations.

C. Degradate toxicity

One of the degradation products of malathion under selected environmental conditions is the oxon of the molecule, malaoxon. Limited toxicity data for the malaoxon are available for selected taxonomic groups. Table 5 presents available toxicity data for malaoxon for aquatic organisms. No acute or chronic malaoxon toxicity data were available for terrestrial vertebrates.

Table 5. Aquatic organism malaoxon toxicity studies (sourced from ECOTOX studies meeting minimum quality for database and OPP).

Species Tested	Duration Hours	EC_{50} or LC_{50} µg/L	Reference MRID or ECOTOX	Classification
African clawed frog *Xenopus laevis.*	96	900	Snawder and Chambers, 1989	Supl.
Yellow-legged frog *Rana boylii*	96	23	Sparling and Fellers, 2007	Supl.
Medaka *Oryzias latipes*	48	280	Tsuda et al., 1997	Supl.
Carp *Cyprinus carpio*	48	1600	Gantberg et al., 1989	Supl.
Perch *Perca fluviatilis*	48	150	Gantberg et al., 1989	Supl.
Roach *Rutilus rulitus*	48	1100	Gantberg et al., 1989	Supl.
Midge *Chironomus riparius*	24	5.4	Hoffman, 1995	Supl.

There are a limited number of situations where acute toxicity for malathion and malaoxon have been determined for the same test species (Table 6). In most cases malaoxon is observed to be more toxic than malathion. The strongest comparison of relative potencies within these species is with the larval yellow-legged frog tests, which were conducted in the same lab with the same stock organisms. Because this comparison has the highest degree of confidence and is the most conservative, the potency ratio of 92.9 malathion to malaoxon will be used to adjust other effects endpoints for malathion to malaoxon potency equivalency.

Table 6. Within species comparisons of malathion and malaoxon acute toxicity.

Species Tested	Malathion LC_{50} µg/L	Malaoxon LC_{50} µg/L	Ratio of Malathion to Malaoxon Toxicity
Carp *Cyprinus carpio*	6590 - 23180	1600	4.1 – 14.5
Medaka *Oryzias latipes*	1800	280	6.4
Yellow-legged frog *Rana boylii*	2137	23	92.9
Midge *Chironomus riparius*	1.9 - 440	5.4	0.35 – 81.5

The only exception to the application of the above relative potency adjustment factor will be for plants, where the mechanism of action is not likely to be related to the anti-acetyl

cholinesterase activity of the phosphate ester or thioester of malaoxon or malathion. Therefore, in this case of plant toxicity prediction malathion and malaoxon will be assumed to be equipotent.

The registrant has submitted additional toxicity data on the acute toxicity of malathion degradation products to aquatic organisms. These studies, along with the results reported by the study authors, are listed in Table 7. These studies have not yet been reviewed by the Agency. The Agency will review these studies as part of registration review process and determine their acceptance classification. Until they are reviewed, the results are considered preliminary and subject to change. However, based on preliminary results, malathion dicarboxylic acid and malathion monocarboxylic acid appear to be much less toxic to aquatic organisms than malathion or malaoxon. Being that the mode of action of malathion (inhibition of acetylcholinesterase activity) is similar in both aquatic and terrestrial animals, these degradation products are also expected to have much less toxicity than malathion or malaoxon in terrestrial animals as well.

Table 7. Preliminary toxicity results from unreviewed studies on the ecological effects of malathion degradates to aquatic species and the associated acute toxicity classification.

Taxonomic Group	Test Material	% A.I.	Surrogate Species	Acute Toxicity (preliminary estimate)	MRID, Citation
Freshwater fish	Malathion dicarboxylic acid	98.8	Bluegill sunfish (*Lepomis mcrochirus*)	96-hr LC_{50} > 100 mg/L	47540302 (Gries and Purghart, 2001e)
	Malathion monocarboxylic acid	92.2	Bluegill sunfish (*Lepomis mcrochirus*)	96-hr LC_{50} = 79 mg/L	47540304 (Gries and Purghart, 2001f)
Freshwater invertebrates	Malathion dicarboxylic acid	98.8	Water flea (*Daphnia magna*)	48-hr EC_{50} = 71 mg/L	47540303 (Gries and Purghart, 2001g)
	Malathion monocarboxylic acid	92.2	Water flea (*Daphnia magna*)	48-hr EC_{50} = 3.5 mg/L	47540303 (Gries and Purghart, 2001h)

[1] Based on measured concentration of active ingredient.

D. Ecological Incidents

The Ecological Incident Information System (EIIS) was used to evaluate ecological incidents associated with use of Malathion. Incidents in this database are only ones which have been investigated, linked to one or more pesticide active ingredient, and reported to the Office of Pesticide Programs. We believe that these incidents represent only a fraction of the total number of incidents that have occurred. Incidents in this system are categorized by certainty, which indicates the Agency's judgment on the probability that malathion was the cause of the observed effects. Ecological incidents in the EIIS database are summarized in Table 8 and described in greater detail in Appendix D.

Table 8. Summary of ecological incidents associated with malathion use, by certainty.

Incident Type	Use Type	Certainty				
		All (excluding unlikely)	Unlikely	Possible	Probable	Highly Probable
Aquatic (excluding misuse)	Agricultural sites	10 (9)	1	4	4	1
	Mosquito control	7	0	1	4	2
	Unknown	7	0	4	2	1
	All	24 (23)	1	9	10	4
Aquatic (misuse only)	Agricultural sites	3 (2)	1	0	1	1
	Mosquito control	1	0	1	0	0
	Unknown	2	0	2	0	0
	All	6 (5)	1	3	1	1
Bees	Agricultural sites	5	0	3	0	2
	Unknown	2	0	2	0	0
	All	7	0	5	0	2
Wildlife	Mosquito control	1	0	1	0	0
	Unknown	1	0	1	0	0
	All	2	0	2	0	0
Plants	Agricultural use	2 (1)	1	1	0	0
	Homeowner use	1	0	1	0	0
	Unknown	1	0	1	0	0
	All	4 (3)	1	3	0	0

Excluding incidents associated with misuses and incidents with a certainty level less than "possible", there were 23 incidents in which aquatic animals were killed. All of these incidents involved mortality of fish. One incident also involved death of blue crabs and one incident involved the death of an alligator. Aquatic incidents occurred in both freshwater and saltwater habitats. They were associated with both agricultural uses and mosquito control uses of malathion. For both of these use types, there were numerous incidents with a high certainty level, providing strong evidence that both agricultural and mosquito control use of malathion can cause adverse effects to fish and other aquatic organisms. There were 6 additional aquatic incidents that were associated with known misuses of malathion.

In 1999, the population of the American lobster (*Homarus americanus*) in Long Island Sound suffered a severe mortality event, causing devastating economic damage to the regional lobster fishery. This die-off occurred following extensive aerial spraying of pesticides for vector control in the summer of 1999, which was undertaken in response to a widespread outbreak of West Nile Virus that was occurring at that time in the Northeast. Malathion had been applied in New York. Two pyrethroids (resmethrin and sumithrin) and methoprene were applied in both New York and Connecticut. Extensive

research was undertaken after this event to identify the cause and to determine the role of exposure to these pesticides, if any, in the mortality event. The research ultimately concluded that an outbreak of a parasitic amoebae, *Neoparamoeba pemaquidensis*, was the proximal cause of the lobster mortality, but that multiple other stressors, including pesticide exposure, may have contributed to the die-off by physiologically weakening the lobsters, making their immune response too weak to fend off the disease (Pearce and Balcom, 2005). During the registration review process, the Environmental Fate and Effects Division will analyze findings of the numerous research projects on this topic and will assess the potential contribution of malathion in the causation of this event.

Seven incidents of bee kills were associated with malathion use. In two of these cases, the Agency judged the certainty that malathion was the cause to be "highly probable." Bee kill incidents were associated with use of malathion on alfalfa, cotton, cherry, and unknown use sites. No bee kill incidents were associated with mosquito control use.

Only two incidents associated with malathion use involved mortality of wildlife. For both these incidents, the certainty level was "possible." In both cases, the wildlife were exposed to one or more other pesticide which is highly toxic to wildlife. In one incident involving mortality of 10 fox squirrels, the squirrels also were exposed to zinc phosphide, a rodenticide which frequently causes mortality of nontarget mammals. In the other terrestrial wildlife incident in which 17 western sandpipers were killed, the birds also were exposed to temephos, an insecticide which has much greater toxicity to birds than does malathion. Thus it is uncertain how much exposure to malathion contributed to these mortalities.

In addition to the aquatic and terrestrial animal incidents discussed above, registrants have reported three additional "minor wildlife" (WA) incidents that were associated with malathion. These were reported to the Agency as aggregated counts, and therefore no information is available on the use site associated with these incidents, or on the types of organisms that were involved. There is also no information available to judge the certainty of these incidents.

Four incidents of plant damage have been associated with the use of malathion. One of these was assigned a certainty of "unlikely" and the other three were assigned a certainty of "possible." Of the three with a certainty of "possible," two involved exposure to other pesticides, making the determination of cause uncertain. The third "possible" incident was a complaint from a homeowner that use of a product containing malathion damaged ornamental roses, but this allegation was not verified. In all, the reported plant damage incidents do not provide strong evidence that use of malathion may harm plants.

In conclusion, evidence from reported ecological incidents suggest that use of malathion poses a risk to aquatic organisms and nontarget insects, but does not provide evidence of substantial risk to terrestrial wildlife or plants. These conclusions are consistent with the relative hazard of malathion inferred from laboratory toxicity testing.

E. Ecosystems Potentially at Risk

The ecosystems potentially at risk are often extensive in scope, therefore, it may not be possible to identify specific ecosystems during the development of a nation-wide ecological risk assessment. However, in general terms, terrestrial ecosystems potentially at risk could include the treated field and immediately adjacent areas that may receive drift or runoff. Areas adjacent to the treated field could include cultivated fields, fencerows and hedgerows, meadows, fallow fields or grasslands, woodlands, riparian habitats, and other uncultivated areas.

Aquatic ecosystems potentially at risk include water bodies adjacent to, or down stream from, the treated field and might include impounded bodies such as ponds, lakes and reservoirs, or flowing waterways such as streams or rivers. For uses in coastal areas, aquatic habitat also includes marine ecosystems, including estuaries.

V. Assessment Endpoints

Assessment endpoints represent the actual environmental value that is to be protected, defined by an ecological entity (species, community, or other entity) and its attribute or characteristics (EPA 1998). For malathion, the ecological entities include the following: birds, reptiles, terrestrial-phase amphibians, mammals, freshwater fish, freshwater aquatic-phase amphibians and invertebrates, estuarine/marine fish and invertebrates, terrestrial plants, insects, aquatic plants, and algae. The attributes for each of these entities include growth, reproduction, and survival.

VI. Conceptual Model

For a pesticide to pose an ecological risk, it must reach ecological receptors in biologically significant concentrations. An exposure pathway is the means by which a pesticide moves in the environment from a source to an ecological receptor. For an ecological pathway to be complete, it must have a source, a release mechanism, an environmental transport medium, a point of exposure for ecological receptors, and a feasible route of exposure.

The conceptual model for malathion provides a written description and visual representation of the predicted relationships between malathion, potential routes of exposure, and the predicted effects for the assessment endpoint. A conceptual model consists of two major components: risk hypothesis and a conceptual diagram (USEPA 1998).

As discussed previously, several ecological and endangered species risk assessments have been conducted by EFED for malathion, including a national level risk assessment

supporting the RED (USEPA 2006), an assessment of the risks of malathion to the California red-legged frog, a Federally-listed threatened species (USEPA 2007). An endangered species assessment has also been conducted by the Agency's Field and External Affairs Division (FEAD) for exposures of malathion to the Pacific Anadromous Salmonids (USEPA 2004*a*). These previous assessments and more recent data serve as a basis for the risk hypothesis and conceptual model developed for current registered uses of malathion.

A. Risk Hypothesis

A risk hypothesis describes the predicted relationship among the stressor, exposure, and assessment endpoint response along with the rationale for their selection. For malathion, the following ecological risk hypothesis is being employed for this national-level ecological risk assessment:

> *Malathion, when used in accordance with current labels may result in adverse effects upon the survival, growth, and reproduction of non-target terrestrial and aquatic organisms. These nontarget organisms include Federally-listed threatened and endangered species.*

B. Conceptual Diagram

The environmental fate properties of malathion along with monitoring data identifying its presence in surface waters, air and precipitation, indicate that runoff, spray drift, volatilization and atmospheric transport and deposition represent potential transport mechanisms of malathion to aquatic and terrestrial organisms. For malathion, spray drift exposure to aquatic ecosystems includes deposition from applications for adult mosquito control, which are frequently intentionally made over water bodies, as well as off site drift from agricultural uses. These transport mechanisms and resulting movement of malathion into aquatic habitats (water) and terrestrial habitats (soil and foliage) depicted in Figures 2 and 3, respectively. These figures also depict direct and indirect exposure pathways for a broad range of biological receptors of concern (nontarget animals) and the potential attribute changes, *i.e.*, effects such as reduced survival, growth and reproduction, that may occur in the receptors due to malathion and malaoxon exposure. Because malathion is not very lipophilic ($\log k_{ow} = 2.29$) and is metabolized relatively rapidly in organisms, exposure to aquatic organisms through the diet is predicted to be small compared to uptake through the gills and integument, and thus contribute little to ecological risk in aquatic ecosystems.

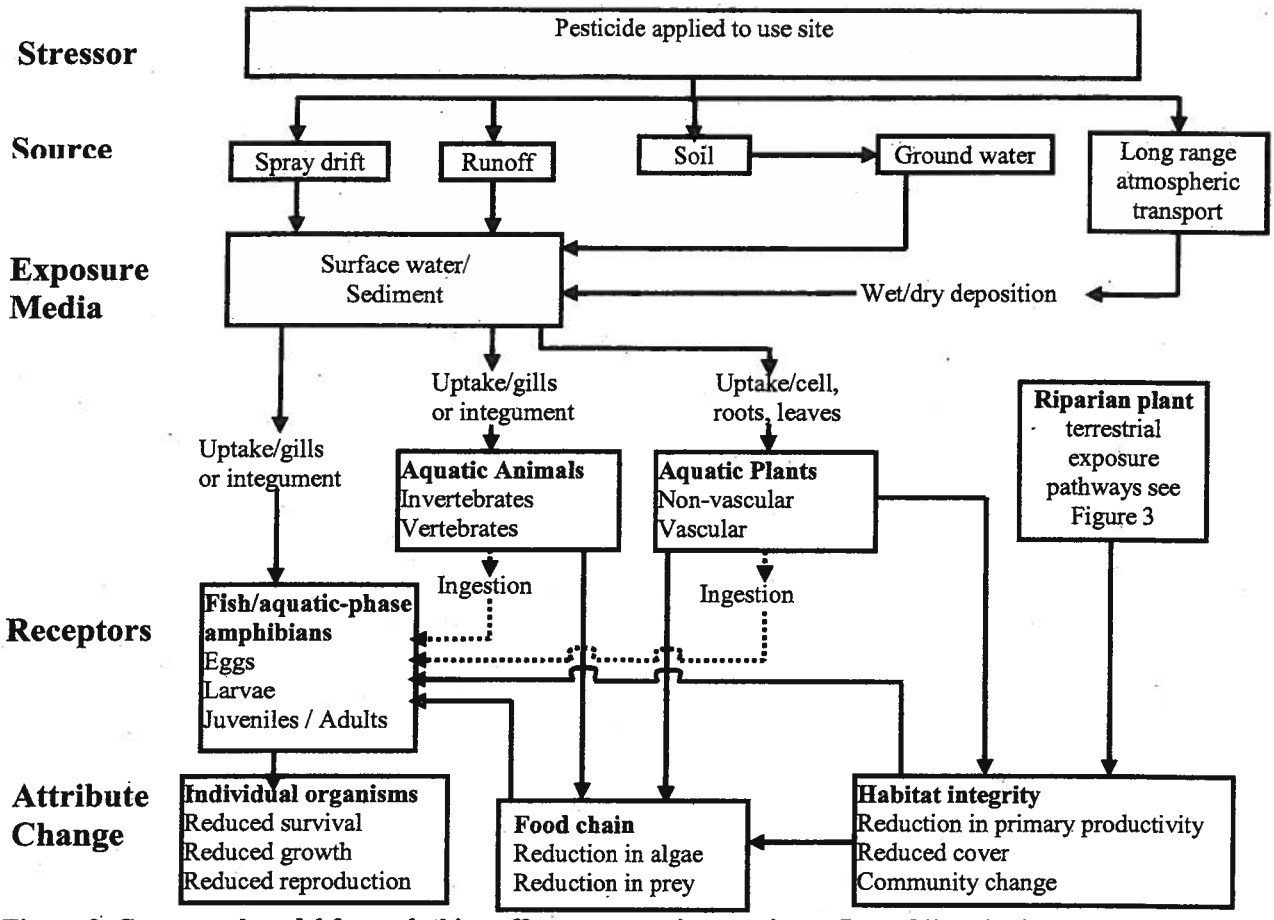


Figure 2. Conceptual model for malathion effects on aquatic organisms. Dotted lines indicate exposure pathways that are expected to have a relatively small contribution to ecological risk. The spray drift from mosquito adulticide applications near or aerially applied over water bodies could be considered a direct application to water.

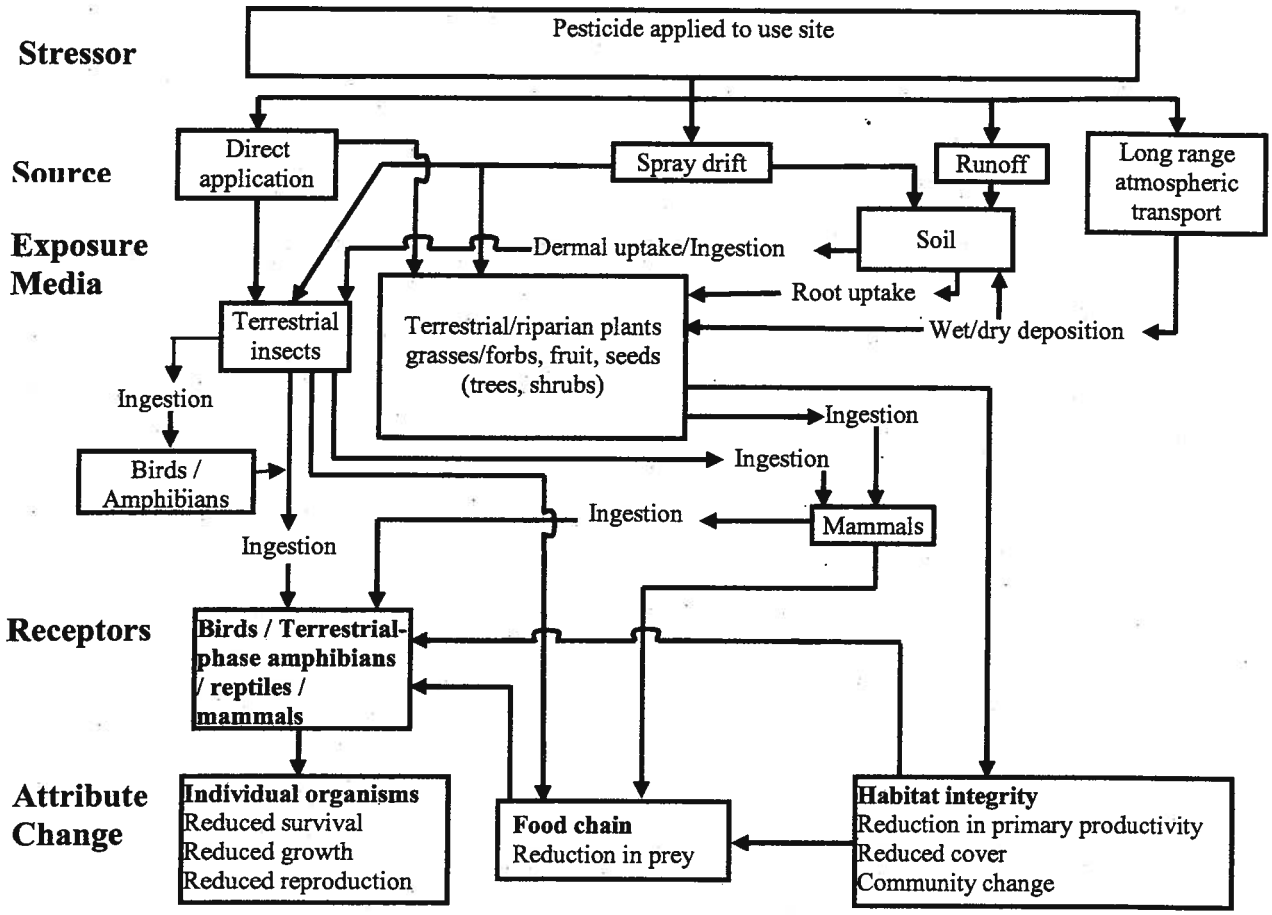


Figure 3. Conceptual model for malathion effects on terrestrial organisms.

Malaoxon was most recently assessed in the CRLF assessment (USEPA 2007). Because of the lack of fate data for malaoxon and because of structural similarity to malathion, most of the fate properties of malathion were assumed to be similar for malaoxon. The only fate properties changed for malaoxon were the molecular weight (314.29 g/mol) and Koc (46 L/kg). Application rates were assumed to be 1.8% of the malathion application rates (the highest reported malaoxon conversion rate in any of the fate studies). This assessment of risk for malaoxon was highly uncertain due to the many assumptions involved. For this reason, a complete set of fate and effects data has been requested in this problem formulation document.

VII. Analysis Plan

In order to address the risk hypothesis, the potential for adverse effects on the environment is estimated. The use, environmental fate, and ecological effects of malathion are characterized and integrated to assess the risks. This is accomplished using a risk quotient (ratio of exposure concentration to effects concentration) approach. Although risk is often defined as the likelihood and magnitude of adverse ecological effects, the risk quotient-based approach does not provide a quantitative estimate of

likelihood and/or magnitude of an adverse effect. However, as outlined in the Overview Document (USEPA 2004*b*), the likelihood of effects to individual organisms from particular uses of malathion is estimated using the probit dose-response slope and either the level of concern (discussed below) or actual calculated risk quotient value.

This analysis plan will be revisited and may be revised depending upon the information submitted by the public in response to the opening of the Registration Review docket for malathion.

A. Stressors of Concern

The stressors of concern for this assessment include malathion and malaoxon. Exposures in aquatic and terrestrial habitats will be estimated for both malathion and malaoxon.

As discussed in Appendix A, the primary degradate of malathion in terms of quantity produced is malathion carboxylic acid (MCA), which is formed by the hydrolysis of the parent. Comparison of available toxicity information for MCA and malathion have shown that MCA is much less toxic than malathion. Therefore, EFED does not intend to assess the degradate MCA in the registration review document at this time because the risks associated with this degradate are expected to be considerably lower than from the parent or oxon degradate.

Malathion also transforms in the environment to its oxygen analog, malaoxon. Oxon analogs of organophosphate insecticides are typically more potent inhibitors of acetylcholinesterase than are the parent compounds. Available data indicate that malaoxon is approximately 93 times more toxic to amphibians than the parent compound (Sparling and Fellars 2007). Also, based on mammalian toxicity and Benchmark Dose (BMD) modeling, the agency estimated that malaoxon is approximately 22 times more toxic than the parent compound in mammals (USEPA 2006*a*). Submitted environmental fate studies for malathion typically do not identify malaoxon as it does not comprise >10% of residues, indicating that it is not expected to be a major degradate of malathion in aquatic and terrestrial environments. However, malaoxon has been detected in runoff and surface water samples, indicating that it is present in the environment. Little laboratory data are available to estimate the formation and decline of malaoxon; therefore, it is only possible to estimate aquatic exposures by using conservative assumptions.

Evaluation of pesticide mixtures is beyond the scope of this assessment because of the myriad factors that cannot be quantified based on the available data. Those factors include identification of other possible co-contaminants and their concentrations, differences in the pattern and duration of exposure among contaminants, and the differential effects of other physical/chemical characteristics of the receiving waters (*e.g.* organic matter present in sediment and suspended water). Evaluation of factors that could influence additivity/synergism is beyond the scope of this assessment and is beyond the capabilities of the available data to allow for an evaluation. However, it is acknowledged that not considering mixtures could over- or under-estimate risks depending on the type

of interaction and factors discussed above. The assessment will however, analyze the toxicity of formulated products (including formulations involving more than one active ingredient) and will determine whether formulated products are more toxic than the technical grade active ingredient data used for assessing both direct and indirect risks.

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) *"may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate."* Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there were scientific bases for including, as part of the program, androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. When the appropriate screening and/or testing protocols being considered under the Agency's Endocrine Disrupter Screening Program (EDSP) have been developed and vetted, malathion may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption. For further information on the status of the Endocrine Disrupter Screening Program please visit our website: http://www.epa.gov/endo/.

B. Measures of Exposure

In order to estimate risks of malathion exposures in aquatic and terrestrial environments, all exposure modeling and resulting risk conclusions will be based on maximum application rates and methods cited in Appendix Table B1 and will be estimated for each use of malathion. Measures of exposure are based on aquatic and terrestrial models that predict estimated environmental concentrations (EECs) of malathion. The models used to predict aquatic EECs are the Pesticide Root Zone Model coupled with the Exposure Analysis Model System (PRZM/EXAMS). The model used to predict terrestrial EECs on food items is T-REX. The model used to derive EECs relevant to terrestrial and wetland plants is TerrPlant. These models are parameterized using relevant reviewed environmental fate data from registrant submissions and the literature; PRZM/EXAMS model input values will be consistent with the most recent version of the input parameter guidance (USEPA 1998).

PRZM (v3.12.2, May 2005) and EXAMS (v2.98.4.6, April 2005) are simulation models coupled with the input shell pe5.pl (Aug 2007). The models generate daily exposures and calculated 1-in-10 year EECs of malathion that may occur in surface water bodies adjacent to application sites receiving malathion through runoff and spray drift. PRZM simulates pesticide application, movement, and transformation on an agricultural field and the resultant pesticide loadings to a receiving water body via runoff, erosion and spray drift. EXAMS simulates the fate of the pesticide in the water body and estimates resulting concentrations. The standard scenarios used for ecological pesticide assessments assume application to a 10-hectare agricultural field that drains into an

adjacent 1-hectare water body that is 2 meters deep (20,000 m^3 volume) with no outlet. PRZM/EXAMS is used to estimate screening-level exposure of aquatic organisms to malathion. The measure of exposure for aquatic species is the 1-in-10 year return peak or rolling mean concentration. The 1-in-10 year peak is used for estimating acute exposures of direct effects to aquatic organisms. The 1-in-10-year 60-day mean is used for assessing chronic exposure to fish and aquatic-phase amphibians. The 1-in-10-year 21-day mean is used for assessing chronic exposure to aquatic invertebrates.

Exposure estimates for terrestrial animals assumed to be in the target area or in an area exposed to spray drift are derived using the T-REX model (version 1.4.1, 10/09/2008). This model incorporates the Kenega nomograph, as modified by Fletcher *et al.* (1994), which is based on a large set of field residue data. The upper limit values from the nomograph represent the 95th percentile of residue values from actual field measurements (Hoerger and Kenega 1972). The Fletcher *et al.* (1994) modifications to the Kenega nomograph are based on measured field residues from 249 published research papers, including information on 118 species of plants, 121 pesticides, and 17 chemical classes. EECs for terrestrial plants inhabiting dry and wetland areas are derived using TerrPlant (version 1.2.2, 12/26/2006). This model uses estimates of pesticides in runoff and in spray drift to calculate EECs. EECs are based upon solubility, application rate and minimum incorporation depth.

Two spray drift models, AgDisp and AgDRIFT are used to assess exposures of terrestrial plants to malathion deposited in terrestrial habitats by spray drift. AgDrift (version 2.01; dated 5/24/2001) (Teske *et al* 2001) is used to simulate ground, aerial, and spray blast applications. To estimate potential spray drift deposition at distances that exceed 1000 feet, AGDisp (version 8.13; dated 12/14/2004) (Teske and Curbishley 2003) is used, which simulates aerial and ground applications using a Gaussian far-field extension.

At this time, the Agency does not have an approved model for estimating atmospheric transport of pesticides and resulting exposure to organisms in areas receiving pesticide deposition from the atmosphere. Methods to describe the contributions of atmospheric transport and deposition of malathion and malaoxon to exposures to non-target organisms will be explored and incorporated into this risk assessment as part of registration review of malathion.

C. Measures of Effect

Ecological effect data are used as measures of direct and indirect effects to biological receptors. Data were obtained from registrant-submitted studies or from literature studies identified by ECOTOX. The ECOTOXicology database (ECOTOX) was searched in order to provide more ecological effects data to bridge existing data gaps. ECOTOX is a source for locating single chemical toxicity data and potential chemical mixture toxicity data for aquatic life, terrestrial plants, and wildlife. ECOTOX was created and is maintained by the USEPA, Office of Research and Development, and the National Health and Environmental Effects Research Laboratory's Mid-Continent Ecology Division (http://cfpub.epa.gov/ecotox/).

Information on the potential effects of malathion on non-target animals is also collected from the Ecological Incident Information System (EIIS). The EIIS is a database containing adverse effect (typically mortality) reports on non-target organisms where such effects have been associated with the use of pesticides.

Where available, sublethal effects observed in both registrant-submitted and open literature studies will be evaluated qualitatively. Such effects have included behavioral changes (*e.g.*, lethargy, changes in coloration and effects olfaction). Quantitative assessments of risks, though, are limited to those endpoints that can be directly linked to the Agency's assessment endpoints of impaired survival, growth, and reproduction.

The assessment of risk for direct effects to non-target organisms makes the assumption that toxicity of malathion to birds is similar to terrestrial-phase amphibians and reptiles. The same assumption is made for fish and aquatic-phase amphibians.

The acute measures of effect used for animals in this screening-level assessment are the LD_{50}, LC_{50} and EC_{50}. LD stands for "Lethal Dose", and LD_{50} is the amount of a material, given all at once, that is estimated to cause the death of 50% of the test organisms. LC stands for "Lethal Concentration" and LC_{50} is the concentration of a chemical that is estimated to kill 50% of the test organisms. EC stands for "Effective Concentration" and the EC_{50} is the concentration of a chemical that is estimated to produce a specific effect in 50% of the test organisms. Endpoints for chronic measures of exposure for listed and non-listed animals are the NOAEL/NOAEC and NOEC. NOAEL stands for "No Observed-Adverse-Effect-Level" and refers to the highest tested dose of a substance that has been reported to have no harmful (adverse) effects on test organisms. The NOAEC (*i.e.*, "No-Observed-Adverse-Effect-Concentration") is the highest test concentration at which none of the observed effects were statistically different from the control. The NOEC is the No-Observed-Effects-Concentration. For non-listed plants, only acute exposures are assessed (*i.e.*, EC_{25} for terrestrial plants and EC_{50} for aquatic plants); for listed plants, either the NOAEC or EC_{05} is used.

In the absence of data for either acute or chronic effects, the conservative assumption will be to presume that malathion is toxic.

D. Integration of Exposure and Effects

Risk characterization is the integration of exposure and ecological effects characterization to determine the potential ecological risk from the use of malathion on fruits, nuts, vegetables and ornamentals, and the likelihood of direct and indirect effects to non-target organisms in aquatic and terrestrial habitats. The exposure and toxicity effects data are integrated in order to evaluate the risks of adverse ecological effects on non-target species. For the assessment of malathion risks, the risk quotient (RQ) method is used to compare exposure and measured toxicity values. EECs are divided by acute and chronic toxicity values. The resulting RQs are then compared to the Agency's levels of concern (LOCs) (USEPA 2004*b*). These criteria are used to indicate when malathion's uses, as directed on the label, have the potential to cause adverse direct or indirect effects to non-target organisms. As noted previously, where data are lacking on the toxicity of malathion, risk will be presumed.

1. Deterministic and Probabilistic Assessment Methods

The quantitative assessment of risk will primarily depend on the deterministic point-estimate based approach described in the risk assessment. An effort will be made to further quantitatively describe potential risks using probabilistic tools that the Agency has developed. These tools have been reviewed by FIFRA Scientific Advisory Panels and have been deemed as appropriate means of refining assessments where deterministic approaches have identified risks that exceed concern levels.

E. Endangered Species Assessments

Consistent with the Agency's responsibility under the Endangered Species Act (ESA), EPA will evaluate potential risks to Federally-listed threatened and/or endangered (listed) species from registered uses of malathion. This assessment will be conducted in accordance with the Overview Document (USEPA 2004*b*), provisions of the ESA, and the Services' *Endangered Species Consultation Handbook* (USFWS/NMFS 1998).

The assessment of effects associated with registrations of malathion is based on an action area. The action area is considered to be the area directly or indirectly affected by the federal action, as indicated by the exceedance of Agency Levels of Concern (LOCs) used to evaluate direct or indirect effects. The Agency's approach to defining the action area under the provisions of the Overview Document (USEPA 2004*b*) considers the results of the risk assessment process to establish boundaries for that action area with the understanding that exposures below the Agency's defined LOCs constitute a no-effect threshold. For the purposes of this assessment, attention will be focused on the footprint of the action (*i.e.*, the area where malathion application occurs), plus all areas where offsite transport (*i.e.*, spray drift, runoff, long-range atmospheric transport, etc.) may result in potential exposure that exceeds the Agency's LOCs. Specific measures of ecological effect that define the action area for listed species include any direct and indirect effects and/or potential modification of its critical habitat, including reduction in

survival, growth, and reproduction as well as the full suite of sublethal effects available in the effects literature. Therefore, the action area extends to a point where environmental exposures are below any measured lethal or sublethal effect threshold for any biological entity at the whole organism, organ, tissue, and cellular level of organization. In situations where it is not possible to determine the threshold for an observed effect, the action area is not spatially limited and is assumed to be the entire United States.

On November 18, 2008, the National Oceanic Atmospheric Administration National Marine Fisheries Service (NMFS) issued a final biological opinion on the effect of pesticide products containing malathion, chlorpyrifos, or diazinon on 28 listed Pacific salmonids (NMFS 2008). Conclusions of this opinion are discussed in section B.4. of this document. During the registration review process, the Agency will be reviewing this opinion and will address risks to Pacific salmonids that were identified as being related to registration of pesticide products containing malathion.

F. Preliminary Identification of Data Gaps

1. Fate

Although many submissions have been made to provide data on the environmental fate of malathion and its degradates, several data gaps exist (Table 5). The data gaps are discussed below. A data call in (DCI) was issued June 2, 2004 to obtain data to fulfill some of these data gaps for malathion and its degradates. The specific components of the DCI are also discussed below.

One of the major areas of uncertainty associated with the fate of malathion in the environment involves the formation and persistence of its oxygen analog, malaoxon (PC Code 657701, CAS No. 1634-78-2). As discussed above, malaoxon was not reported as a major degradate of malathion, *i.e.*, did not constitute greater than 10% of total residues, in any of the available laboratory fate studies. However, malaoxon has been detected in surface waters, air and precipitation and is also known to form during water treatment. The conditions necessary for the formation of malaoxon and its persistence in the environment are not fully understood. Data collected by CaDPR suggests that environments inhospitable to microbial degradation such as inorganic surfaces such concrete may allow malathion to persist for a longer time after application. Data from the medfly eradication program suggests that malaoxon may also similarly persist much longer durations and at higher concentrations. Since data indicate that malaoxon has the potential to be as toxic as or more toxic than malathion, the lack of malaoxon fate data represents a gap in the overall understanding of potential risks associated with uses of malathion. Future assessments of malathion will involve exploration of degradation pathways leading to formation and transport of malaoxon in the environment.

Submission of any available information relevant to the circumstances resulting in the formation, persistence and transport of malaoxon in the environment would greatly reduce the uncertainties associated with the environmental fate of malathion and its degradate of toxicological concern, *i.e.* malaoxon. Of particular interest would be the

identification of pathways of formation for malaoxon in the environment (USEPA 2009). In cases where data are unavailable for the formation of malaoxon in the environment, conservative assumptions will be made to estimate exposure concentrations for malaoxon.

a. Summary of Fate Studies that EFED recommends the Agency request

i. Malathion

Degradation: Aerobic aquatic metabolism study (acidic conditions).
Malathion is generally non-persistent, however EFED lacks important information to evaluate the behavior of malathion under acidic aquatic conditions which might likely increase its persistence and alter degradates produced. To adequately determine the environmental fate of malathion and its degradates aerobic aquatic metabolism data under acidic soil and water conditions are needed.

EFED also requests additional information on environmental malaoxon production. Malathion is used in a large number of settings including more than 60 terrestrial field uses, as well as outdoor residential uses including mosquito, Mediterraean fruitfly, and urban pest control uses, and therefore is exposed to a large variety of environmental conditions. This extensive use under various environmental conditions is likely to result in significant exposure of nontarget organisms to malathion breakdown products from various routes of transformation. Exposures to humans and wildlife may occur through contamination of food, water, and air (by suspended particles) which can result from off-target drift, runoff, and direct application.

Malaoxon Formation: Malathion degradation and malaoxon production in an aerobic soil metabolism study (162-1) using a soil with a low moisture content (<1%) and low organic content (<1%).
The State of California EPA has published a study describing malaoxon production on low organic content soil (0.6%) with a moisture content less than 1% (CaEPA 1993) showing higher malathion production than registrant submitted studies using soils with higher organic (2-2.7%) and moisture (75% of water holding capacity, capacity not stated) content. From the CaEPA data it appears that malaoxon production is favored on dry soils and thus may represent a higher risk scenario for malaoxon production and runoff. EFED believes that data on dry soils may be useful to assess malathion and malaoxon fate and persistence in some use settings which are not ideal for malathion degradation, thus EFED requests the submission of data on malathion degradation and malaoxon production in an aerobic soil metabolism study (162-1) using a soil with a low moisture content (<1%) and low organic content (<1%).

Malaoxon Formation: Malathion degradation and malaoxon production on hard surfaces
It is clear that under many circumstances malathion degrades rapidly to compounds of lower toxicity, usually through microbial metabolism and hydrolysis. However in

residential uses (*e.g.* aerial and ground application for mosquito control) it is likely that malathion will contact dry, microbially inactive and low organic content surfaces such as concrete, asphalt, dry soil, roofing material, and glass. It is expected that malaoxon production will be increased on these surfaces as malathion is exposed to air for extended periods until it is washed away by rain. This is supported by malaoxon monitoring data in urban streams after residential malathion treatment showing similar or higher levels of malaoxon than malathion in some instances (CaDFG 1982). Thus, EFED proposes that malathion persistence and degradation on anthropogenic surfaces be examined (suggestions from the registrant are invited for particular surfaces to be examined). The State of California EPA has published two studies describing adequate methods for determining malaoxon production on dry soil (CaEPA 1993) and steel sheets (CaEPA 1996) which would be amenable to other abiotic surfaces. Both of these studies showed higher malaoxon production than registrant submitted studies, however, but maximal levels of malaoxon production were not achieved. On the steel surface a rainfall event removed most of the malathion after only 2 days. On the dry soil malaoxon production did not decrease by the time the study was terminated at 22 days. Runoff of residential malathion and malaoxon greatly increases risk of human and aquatic wildlife exposure through drinking water and habitat contamination and increase the need for this information. A study of malaoxon production on dry surfaces was required in a separate but forthcoming DCI.

ii. Environmental Fate of Malaoxon

Presently EFED has no registrant submitted fate data for malaoxon. Monitoring data suggest that malaoxon production is an important issue in residential areas. In addition to data on the basic physical properties of malaoxon (solubility, partition coefficient, vapor pressure) EFED requests that the following laboratory studies be submitted for malaoxon based on the brief justification provided. Data from these studies are expected to be sufficient to perform basic fate and exposure modeling of malaoxon.

Degradation

161-1 (hydrolysis). Malathion hydrolysis is an important route of dissipation under alkaline conditions. The phosphorothiolate ester bond of malaoxon may be more susceptible to cleavage via hydrolysis than the analogous phosophorodithioate ester in malathion.

Metabolism

162-1 (aerobic soil). The primary route of malathion degradation on soil is through aerobic metabolism. An open literature study (Paschal and Neville 1976) suggests malaoxon persistence may be greater on soils. Additionally, CaEPA studies have shown levels of malaoxon production exceeding 10% in certain dry, low organic content soils.

162-4 (aerobic aquatic). Although little or no malaoxon production is observed in registrant submitted aquatic studies, malaoxon has been detected in surface waters and the potential for malaoxon runoff may be heightened relative to malathion because it is expected to have higher solubility. Aerobic aquatic metabolism contributes greatly to

malathion degradation. This study was included in a forthcoming DCI (Miederhoff, 2009, personal communication).

Mobility

163-1 (leaching/adsorption/desorption). EFED is not aware of reports of malaoxon groundwater contamination, however, malathion has contaminated groundwater in several states and has the potential to contaminate surface water through runoff. The increased polarity of malaoxon due to the substitution of oxygen for sulfur increases the expected potential of this chemical to be mobile in soil.

2. *Effects*

All data requirements for toxicity testing of the effects of malathion to terrestrial birds and mammals have been fulfilled, but data gaps still exist for the effects of malaoxon on birds and for effects of malathion and malaoxon on aquatic species (Table 10). These include: the fish early life-stage test with a saltwater species (850.1400) and the aquatic invertebrate life cycle test (850.1350). Aquatic toxicity tests with the typical end-use product (TEP) which were previously required for products that contain a mixture of malathion and methoxychlor (USEPA 2006a) are no longer required because all uses of methoxychlor have been cancelled.

Being an organophosphate insecticide, malathion is not expected to have significant toxicity to nontarget plants. The Agency is aware of no data that indicates malathion will significantly effect the growth and reproduction of plants at environmentally relevant exposure levels. Therefore, toxicity testing with aquatic and terrestrial plants are not required.

Literature data indicate that malaoxan, a transformation product of malathion, is more toxic to aquatic organism than the parent compound. Therefore, submission of guideline studies on the toxicity of malaoxon to freshwater and saltwater fish and aquatic invertebrates would be valuable to ecological risk assessment. Data requirements for assessing ecological effects are further described in Section 9.6.

Table 9. Available ecological effects data for terrestrial animals exposed to technical malathion and remaining data gaps.

158 Guideline # (OPPTS)	Requirement Description	Test Species	Are Data Available for Risk Assessment?	MRID	Study Classification
Birds and Mammals					
71-1 (850.2100)	Avian oral toxicity	Mallard duck	Yes	00160000	Acceptable
		Ring-necked pheasant	Yes	00160000	Supplemental
		Horned lark	Yes	00160000	Supplemental
71-2 (850.2200)	Avian dietary toxicity	Northern bobwhite	Yes	00022923	Acceptable
		Mallard	Yes	00022923	Acceptable
		Ring-necked pheasant	Yes	00022923	Acceptable
		Japanese quail	Yes	00022923	Acceptable
71-3 (850.2400)	Wild mammal	--	Not Required	--	--
71-4 (850.2300)	Avian reproduction	Northern bobwhite	Yes	43501501	Acceptable
		Mallard	Yes	42782101	Acceptable
Beneficial Insects					
141-1 (850.3020)	Honeybee acute contact toxicity	Honeybee	Yes	05004003	Acceptable
		Honeybee	Yes	05001991	Acceptable
		Honeybee	Yes	00001999	Acceptable
		Honeybee	Yes	05004151	Acceptable
141-2 (850.3030)	Honeybee toxicity of residues on foliage	Honeybee	Yes	41208001	Acceptable
		Honeybee	Yes	41284701	Acceptable
141-5 (850.3040)	Field testing for pollinators	Honeybee	No Reserved	--	--
Fish					
72-1 (850.1075)	Freshwater fish acute toxicity	Bluegill sunfish	TBD[1]	47540304	TBD[1]
		Rainbow trout	TBD[1]	47540302	TBD[1]
		(Multiple)	TBD[1]	40098001 (Mayer and Ellersieck, 1986)	TBD[1]
72-3 (a) (850.1075)	Marine/estuarine fish acute toxicity (TGAI)	Sheepshead minnow	Yes	41174301	Acceptable
72-3 (d) (850.1075)	Marine/estuarine fish acute toxicity (TEP)	Sheepshead minnow	Yes	41252101	Acceptable
72-4 (a) (850.1400)	Fish early life-stage (freshwater)	Rainbow trout	Yes	41422401	Acceptable
72-4 (a) (850.1400)	Fish early life-stage (saltwater)	--	No[2] Required	--	--
72-5 (850.1500)	Fish life cycle	--	No Reserved	--	--
Aquatic Invertebrates					
72-2 (a) (850-1010)	Freshwater invertebrate acute toxicity (TGAI)	Water flea	TBD[1]	47540303	Not reviewed
		(Multiple)	TBD[1]	40098001 (Mayer and Ellersieck, 1986)	Supplemental?
72-2 (b) (850-1010)	Freshwater invertebrate acute toxicity (TEP)	Water flea	Yes	41029701	Acceptable

158 Guideline # (OPPTS)	Requirement Description	Test Species	Are Data Available for Risk Assessment?	MRID	Study Classification
72-3(b) (850.1025) (850.1055)	Bivalve acute toxicity (TGAI, shell deposition or embryo larvae)	Eastern oyster	TBD	40228401 (Mayer, 1986)	Supplemental?
72-3(c) (850.1035) (850.1045)	Crustacean acute toxicity (TGAI, mysid or penaeid)	Mysid	Yes	41474501	Acceptable
72-3(b) (850.1025) (850.1055)	Bivalve acute toxicity (TEP, shell deposition or embryo larvae)	Eastern oyster	No[3] Not Required	41320201 42249901	Supplemental Invalid
72-3(c) (850.1035) (850.1045)	Crustacean acute toxicity (TEP, mysid or penaeid)	--	No[3] Not Required	--	--
72-4(b) (850.1300)	Aquatic invertebrate life cycle (freshwater)	Water flea	Yes	41718401	Acceptable
72-4(b) (850.1350)	Aquatic invertebrate life cycle (saltwater)	--	No[4] Required	--	--
Sediment Toxicity					
850.1735	Whole sediment: acute freshwater invertebrates	--	No Not Required	--	--
850.1740	Whole sediment: acute marine invertebrates	--	No Not Required	--	--

[1] The acceptability of the available data for this guideline has yet to be determined.
[2] No data have been submitted for this guideline. Results from chronic testing with the red drum reported in Alvarez (2005) could be used as a conservative estimate of chronic toxicity to marine/estuarine fish in the absence of additional data.
[3] Acceptable data has not been submitted to fulfill this guideline requirement. However, testing with freshwater invertebrates indicate that the to invertebrates of malathion TGAI is greater than that of this TEP. The TEP test requirement for a saltwater invertebrate is therefore waved.
[4] No data have been submitted for this guideline.

9.6 Anticipated Data Needs

9.6.1 Environmental Fate and Exposure

Study Title: Modified aerobic aquatic metabolism
Guideline Number: 835.4300; 162-4
Test Substance: Malathion

Rationale for Requiring the Data

Per 40 CFR part 158, which was promulgated on October 26, 2007, an aerobic aquatic metabolism study is required due to malathion being applied to terrestrial crops. Aerobic aquatic metabolism studies facilitate an understanding of a compound's degradation in the water column or sediment under aerobic (oxygen-rich) conditions in the laboratory. These studies are generated by pesticide interaction with microorganisms in a water/sediment system.

Malathion is generally non-persistent, however EFED lacks important information to evaluate the behavior of malathion under acidic aquatic conditions which might likely increase its persistence and alter degradates produced. The major concern is that the existing aerobic aquatic metabolism studies (MRID 42216301 and 43163301) were performed at pHs where hydrolysis would predominate over aerobic aquatic metabolism. To adequately determine the environmental fate of malathion and its degradates, aerobic aquatic metabolism data under acidic soil and water conditions (pH approximately 5.5 to 6.5) are needed.

The fate of malathion and its degradates reaching water bodies through runoff and transformation cannot be fully characterized without the requested data. The requested data would allow EPA to refine its estimates of drinking

water exposure and of acute risk (mortality) and chronic risk (growth and reproduction) estimates for aquatic and estuarine/marine organisms, and allow it to define an action area for endangered species. Risk mitigation strategies (*e.g.*, determining maximum application rate that results in an RQ below the LOC) cannot be determined with confidence without these data.

Practical Utility of the Data

How will the data be used?
No aerobic aquatic metabolism studies that track the transformation of malathion in acidic aquatic environments are currently available. These data will be used to characterize malathion's persistence as well as formation of the oxon. For quantitative exposure estimation, these data will be used to determine appropriate inputs for simulation modeling.

How could the data impact the Agency's future decision-making?
Without these required data, the fate of malathion cannot be fully characterized and exposure to potentially toxic degradates cannot be quantified. The persistence of malathion and the degradates which may be found in drinking water in acidic environments and to which aquatic organisms will be exposed is uncertain. In the absence of acceptable data, conservative assumptions will be made. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for malathion which are unnecessarily severe.

Study Title: Modified aerobic soil metabolism
Guideline Number: 835.4100; 162-1
Test Substance: Malathion

Rationale for Requiring the Data

Per 40 CFR part 158, which was promulgated on October 26, 2007, an aerobic soil metabolism study is required due to malathion being applied to terrestrial crops. Aerobic soil metabolism studies facilitate an understanding of a compound's degradation in the soil under aerobic (oxygen-rich) conditions in the laboratory.

Malathion is generally non-persistent, however EFED lacks important information to evaluate the behavior of malathion under acidic soil conditions which might likely increase its persistence and alter degradates produced. The major concern is that the existing aerobic soil metabolism studies (MRID 41721701 and 43163301) were performed at pHs where hydrolysis would predominate over aerobic soil metabolism. To adequately determine the environmental fate of malathion and its degradates, aerobic soil metabolism data under acidic soil and water conditions (pH approximately 5.5 to 6.5) are needed.

The fate of malathion and its degradates reaching water bodies through runoff and transformation cannot be fully characterized without the requested data. The requested data would allow EPA to refine its estimates of drinking water exposure and of acute risk (mortality) and chronic risk (growth and reproduction) estimates for aquatic and estuarine/marine organisms, and allow it to define an action area for endangered species. Risk mitigation strategies (*e.g.*, determining maximum application rate that results in an RQ below the LOC) cannot be determined with confidence without these data.

Practical Utility of the Data

How will the data be used?
No aerobic soil metabolism studies that track the transformation of malathion in acidic soils are currently available. These data will be used to characterize malathion's persistence as well as formation of the oxon. For quantitative exposure estimation, these data will be used to determine appropriate inputs for simulation modeling.

How could the data impact the Agency's future decision-making?
Without these required data, the extent of oxon formation cannot be fully characterized and exposure to the oxon degradate cannot be quantified with certainty. The persistence of malathion and formation of the oxon degradates in dry soils that are low in organic matter will be used to characterize potential drinking water exposures and potential exposures to aquatic organisms. In the absence of acceptable data, conservative assumptions will be made. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for malathion which are unnecessarily severe.

Study Title: Aerobic aquatic metabolism
Guideline Number: 835.4300; 162-4

Test Substance: Malaoxon

Rationale for Requiring the Data

Aerobic aquatic metabolism studies facilitate an understanding of a compound's degradation in the water column or sediment under aerobic (oxygen-rich) conditions in the laboratory. These studies are generated by pesticide interaction with microorganisms in a water/sediment system.

Although little or no malaoxon production is observed in registrant submitted aquatic studies, malaoxon has been detected in surface waters and the potential for malaoxon runoff may be heightened relative to malathion because it is expected to have higher solubility. Aerobic aquatic metabolism contributes greatly to malathion degradation. This study was already included in a forthcoming DCI (Miederhoff, 2009, personal communication). However, data have not yet been submitted to the Agency.

The fate of malaoxon reaching water bodies cannot be fully characterized without the requested data. The requested data would allow EPA to refine its estimates of drinking water exposure and of acute risk (mortality) and chronic risk (growth and reproduction) estimates for aquatic and estuarine/marine organisms, and allow it to define an action area for endangered species. Risk mitigation strategies (*e.g.*, determining maximum application rate that results in an RQ below the LOC) cannot be determined with confidence without these data.

Practical Utility of the Data

How will the data be used?

No aerobic aquatic metabolism studies that track the degradation of malaoxon in water are currently available. These data will be used to characterize malaoxon's persistence in water. For quantitative exposure estimation, these data will be used to determine appropriate inputs for simulation modeling.

How could the data impact the Agency's future decision-making?

Without these required data, the fate of malaoxon cannot be fully characterized and exposure cannot be quantified. The persistence of malaoxon in drinking water and other surface waters cannot be fully characterized. In the absence of acceptable data, conservative assumptions will be made. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for malathion which are unnecessarily severe.

Study Title: Aerobic soil metabolism
Guideline Number: 835.4100; 162-1
Test Substance: Malaoxon

Rationale for Requiring the Data

Aerobic soil metabolism studies facilitate an understanding of a compound's degradation in the soil under aerobic (oxygen-rich) conditions in the laboratory.

The primary route of malathion degradation on soil is through aerobic metabolism. An open literature study (Paschal and Neville 1976) suggests malaoxon persistence may be greater on soils. Additionally, CaEPA studies have shown levels of malaoxon production exceeding 10% in certain dry, low organic content soils. Therefore, it is important to understand the dissipation of this toxic degradates.

Practical Utility of the Data

How will the data be used?

These data will be used to characterize the environmental fate and potential exposures to the oxon degradate, which has been shown to be approximately 100-fold more toxic than malathion. For quantitative exposure estimation, these data may be used to determine appropriate inputs for simulation modeling of the oxon degradate.

How could the data impact the Agency's future decision-making?

The persistence of malaoxon in soil will be used to characterize potential drinking water exposures and potential exposures to aquatic organisms. In the absence of acceptable data, conservative assumptions will be made. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for malathion which are unnecessarily severe.

Study Title: Hydrolysis
Guideline Number: 161-1

Test Substance: Malaoxon

Rationale for Requiring the Data

Malathion hydrolysis is an important route of dissipation under alkaline conditions. The phosphorothiolate ester bond of malaoxon may be more susceptible to cleavage via hydrolysis than the analogous phosophorodithioate ester in malathion. This study will provide data on hydrolytic dissipation.

Practical Utility of the Data

How will the data be used?

No acceptable hydrolysis studies are currently available on malaoxon to allow for characterization of the degradation of malaoxon in water. These data will be used to characterize malaoxon's persistence in water. For quantitative exposure estimation, these data will be used to determine appropriate inputs for simulation modeling. Malaoxon has been shown to be considerably more toxic than malathion to aquatic organisms, and these data will allow for characterization of the concentration and duration of potential exposures to the toxic degradates.

How could the data impact the Agency's future decision-making?

Without these data, the fate of malaoxon cannot be fully characterized. Malaoxon may be more susceptible to hydrolysis than malathion. However, without supporting data, conservative assumptions will be made, and the use of malathion may need to be restricted in areas where endangered species could be exposed. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for disulfoton which are unnecessarily severe.

Study Title: Leaching/adsorption/desorption
Guideline Number: 163-1; 835.1230
Test Substance: Malaoxon

Rationale for Requiring the Data

Malathion has contaminated groundwater in several states and has the potential to contaminate surface water through runoff. The increased polarity of malaoxon due to the substitution of oxygen for sulfur increases the expected potential of this chemical to be mobile in soil.

Adsorption/desorption studies facilitate an understanding of a compound's transport in the environment and its partitioning between water and soil/sediment. The fate of malaoxon in soil and water/sediment systems cannot be characterized without the requested data.

Practical Utility of the Data

How will the data be used?

No studies are currently available on malaoxon to allow for characterization of the leaching potential. These data will be used to characterize malaoxon's potential to contaminate ground water. Adsorption/desorption data, along with aerobic soil metabolism data, will allow for direct estimation of expected exposures resulting from conversion to the oxons. In addition, this data will allow the Agency to assess the expected persistence of the oxon in surface waters and its partitioning to sediment for both human health drinking water assessments and ecological risk assessments.

How could the data impact the Agency's future decision-making?

Without these data, conservative assumptions will be made, and the use of malathion may need to be restricted in areas where endangered species could be exposed. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions for disulfoton which are unnecessarily severe.

9.6.2 Ecological Effects

Several effects studies that are currently not available would be valuable to the ecological risk assessment of malathion. These are summarized below. Sediment toxicity studies are not required because the chemical properties do not meet the properties that trigger sediment toxicity studies. A field study of the effect of malathion on bees is not required because the impact of malathion to bees is expected to be from mortality caused by acute

toxicity, rather than from reproductive, developmental, and behavioral effects, and existing data are adequate for characterizing risk from acute toxicity. Furthermore, substantial information on the field effects of malathion are already available through studies published in the scientific literature.

Guideline Number: 850.2100 **Test Substance: Malathion; Malaoxon** **Study Title: Avian acute oral toxicity**
Rationale for Requiring the Data
Required acute oral studies include the following: (1) Malathion: Acute LD50 in Passerine species (2) Malaoxon: Acute LD50 in bobwhite quail or mallard duck AND a passerine species **Rationale**: Acceptable acute oral toxicity data on passerine species are required under 40 CFR Part 158 and have not been submitted for malathion or the oxon transformation product, malaoxon. Additionally, no acute oral mallard duck or bobwhite quail toxicity studies have been submitted on malaoxon. Data on malaoxon are required because oxon analogs of organophosphate pesticides are generally known to be considerably more toxic than parent chemical. Sparling and Fellars (2007) found that malaoxon is approximately 93 times more toxic to amphibians than malaoxon, and the Health Effects Division of EPA estimate that malaoxon is approximately 22 times more toxic to mammals than malathion. Malaoxon is therefore likely to be more toxic than malathion to birds as well. Based on monitoring data collected during the Medfly Eradication Program in California, it is known that maloxon can form in the environment and, therefore, is probably available to wildlife. The Agency does not have any data on the toxicity of malaoxon to birds. In the absence of these data, the Agency cannot quantify the extent that the potential risks from exposure to malaoxon will enhance the potential risks resulting from exposure to parent alone. Also, the effectiveness of mitigation actions (if any are implemented) on potential ecological risks cannot be fully quantified.
Practical Utility of the Data
How will the data be used? These data are necessary to evaluate the extent of potential acute risk to avian species and will be used to calculate acute RQs for birds. They also would be used to assess the potential of adverse effects to threatened and endangered species that might be exposed to malathion. **How could the data change the Agency's decision or impact the Agency's future decision-making?** Based on previous assessments, acute effects from exposure to malathion is expected to pose some risk to birds, with RQ's exceeding the acute LOC only for uses with higher application rates and repeated exposure. Therefore, the decision on which, if any, uses require risk mitigation actions to reduce acute risk to birds is not clearcut. Having data on the acute toxicity of malaoxon would allow us to better quantify the risk to combined exposure of birds to malathion and malaoxon. The additional hazard caused by the presence of malaoxon in the diet and drinking water of birds could enhance the risk enough to change the risk conclusion for acute hazards to birds, and could change the decision on the need for risk mitigation action. Furthermore, the acute toxicity data on malaoxon would allow us to better characterize the risk of acute effects to federally listed threatened and endangered species. Without these data, the magnitude of potential from combined exposure to malathion and malaoxon cannot be quantified. The lack of these data will limit the flexibility that the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions which could be unnecessarily severe. The lack of toxicity data for passerine species would hamper the Agency's ability to characterize the potential risk of malathion to threatened and endangered species of passerine birds.

Guideline Number: 850.1010, 850.1075 **Test Substance: Malaoxon** **Study Title: Freshwater acute toxicity in invertebrates and fish**
Rationale for Requiring the Data
Required acute studies include the following: Acute studies in bluegill sunfish and rainbow trout; acute study in daphnids **Rationale**: Literature data indicate that malaoxan, a degradation product of malathion, is more toxic to aquatic organism than the parent compound. Also, malaoxon has been detected in surface water. Therefore, submission of guideline studies on the toxicity of malaoxon to freshwater fish and aquatic invertebrates would be valuable to ecological risk assessment.
Practical Utility of the Data
How will the data be used? These data are necessary to evaluate the extent of potential acute risks to aquatic species and will be used to characterize the magnitude and duration of potential risks to aquatic species. It would also be used to assess the potential of adverse effects to threatened and endangered fishes that might be exposed to malaoxon. **How could the data change the Agency's decision or impact the Agency's future decision-making?** If future risk assessments are performed without these data, the Agency would assume that malaoxon "may affect" aquatic organisms, which are also used as a surrogate for aquatic amphibians (and listed species from other taxa indirectly). Although potential risks to aquatic organisms is likely to exceed LOCs without submission of such data, the magnitude of potential risks cannot be quantified until these data are submitted. The lack of these data will limit the flexibility that the Agency and registrants have in coming into compliance with the Endangered Species Act and could result in use restrictions which could be unnecessarily severe.

Guideline Number: 850.1400; 850.1500 **Test Substance: Malathion** **Study Title: Life-cycle toxicity in marine/estuarine invertebrate**
Rationale for Requiring the Data
Rationale: No chronic studies have been submitted for malathion in saltwater invertebrates. Based on the use pattern of malathion, exposure to marine/estuarine environments may occur.
Practical Utility of the Data
How will the data be used? These data are necessary to evaluate the extent of potential chronic risks to aquatic species and will be used to characterize the magnitude and duration of potential risks to aquatic species. They would also be used to assess the potential of adverse effects to threatened and endangered invertebrate species that inhabit marine and estuarine environments. **How could the data change the Agency's decision or impact the Agency's future decision-making?** If future risk assessments are performed without these data, the Agency would assume that malathion "may affect" estuarine/marine invertebrates, including shrimp, oysters, and crabs. The Agency would have no data to conduct a chronic screening-level risk assessment for marine/estuarine invertebrates and would not be able to characterize the affect these species, or evaluate the potential for chronic effects to threatened and endangered invertebrates that inhabit marine and estuarine environments.

Guideline Number: 850.1400 **Test Substance: Malathion** **Study Title: Early life-stage toxicity in marine/estuarine fish**
Rationale for Requiring the Data
Rationale: No chronic toxicity studies have been submitted for the effects of malathion on saltwater fish. The only chronic data on the early life-stage toxicity identified in our literature search for malathion is from a study with the red drum discussed in an unpublished Ph.D. dissertation (Alvarez, 2005). This study is not sufficient to fulfill this guideline requirement because it only tested up to 7.4 µ/L, which was not high enough to establish the LOAEC and NOAEC. Based on the use pattern of malathion, exposure to marine/estuarine environments is expected.
Practical Utility of the Data
How will the data be used? These data are necessary to evaluate the extent of potential chronic risks to fish in estuarine and marine environments, and to characterize the magnitude and duration of potential risks to aquatic species. They would also be used to evaluate the potential for malathion to cause adverse effects to threatened and endangered fish that inhabit marine and estuarine habitats. **How could the data change the Agency's decision or impact the Agency's future decision-making?** If future risk assessments are performed without these data, the Agency would not have acceptable data to conduct a RQ analysis for screening risk assessment of potential chronic risk to marine and estuarine fish. Without acceptable data, the Agency would have to rely on chronic risk based on data from a Ph.D. dissertation (Alvarez, 2005), assuming that this study is not found to be invalid. At best, these data would be considered supplemental because the study used different endpoints than the EPA guideline study, and because the study did not determine an LOAEC. Since the study did not test at high enough levels to detect toxic chronic effects, the reported NOAEC from this study is likely conservative (*i.e.*, less than) an NOAEC from a study that would yield both a NOAEC and an LOAEC. Risk conclusions based on this value therefore may be overly conservative. If this study is found to be unacceptable, then the Agency would have no data to conduct a chronic screening-level risk assessment for marine/estuarine fish and would not be able to characterize the affect these species, or evaluate the potential for chronic effects to threatened and endangered fish that inhabit marine and estuarine environments.

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