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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

Date: 20-JUN-2017

SUBJECT: **Oxamyl:** Draft Human Health Risk Assessment in Support of Registration Review.

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Petition No.: NA
Risk Assessment Type: Single Chemical/Aggregate
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DP Barcode: D439443
Registration No.: 352-372; 352-532
Regulatory Action: Registration Review
Case No.: 0253
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1.0 Executive Summary

This assessment has been conducted to support the Registration Review of the insecticide oxamyl. As part of Registration Review, the PRD of Office of Pesticide Programs (OPP) has requested that HED evaluate the hazard and exposure data and conduct dietary and occupational/residential exposure assessments, as needed, to estimate the potential risk to human health that could result from the currently registered uses of oxamyl.

Background

Oxamyl (methyl 2-(dimethylamino)-*N*-[[(methylamino)carbonyl]oxy]-2-oxoethanimidothioate) is an insecticide, acaricide, and nematicide registered for use on a variety of food and feed crops. There are two registered oxamyl end-use product labels: DuPont™ Vydate® L (EPA Reg. #352-372) and DuPont™ Vydate® C-LV (EPA Reg. #352-532). Both products are liquid formulations and are restricted-use products (RUPs). Oxamyl is applied via groundboom sprayer, aerial equipment, airblast sprayer, chemigation, and handheld sprayers. Application rates range from 0.5 to 4 lb ai/acre/day. Oxamyl can be applied from one to eight times a year, depending on the crop. Maximum seasonal application rates range from 2 to 10 lb ai/A. Personal protective equipment (PPE) required on the label includes double layer of clothing, gloves, a chemical-resistant hat for airblast applications, and a PF10 respirator. Both registered product labels currently have restricted entry intervals (REIs) of 48 hours.

Humans may be exposed to oxamyl in food and drinking water since oxamyl may be applied directly to growing crops and applications may result in oxamyl reaching surface and ground water sources of drinking water. There are currently no registered residential uses of oxamyl. Non-occupational exposures may occur as a result of spray drift. In an occupational setting, applicators may be exposed while handling the pesticide prior to application, as well as during application. Occupational post-application dermal exposures may occur when workers enter previously treated agricultural areas. This risk assessment considers all of the aforementioned exposure pathways based on the existing oxamyl uses.

Hazard Assessment

Oxamyl is a member of the *N*-methyl carbamate (NMC) class of pesticides. Like other NMCs, the initiating event in the adverse-outcome pathway (AOP)/mode of action (MOA) for oxamyl is inhibition of the enzyme acetylcholinesterase (AChE). This inhibition leads to an accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system. For NMCs, AChE inhibition (AChEI) occurs via carbamylation of the serine hydroxyl group, which is a reversible binding process allowing for the rapid reactivation of the enzyme. The NMCs, therefore, have a unique MOA that results in rapid onset and recovery of the enzyme. The time to peak inhibition for NMCs is typically between 15 to 45 minutes, while complete recovery of the enzyme is achieved within minutes to hours (US EPA, 2007). Therefore, for NMCs, including oxamyl, repeated daily exposure does not result in increased inhibition of AChE since enzyme recovery is complete before the next acute exposure, and only acute exposure or a series of acute exposures are a concern for neurotoxic effects. As a result, the same endpoint is selected for all durations of an exposure route and short-term assessments are considered protective of intermediate-term assessments. There are no long-term exposures expected for oxamyl. For oxamyl, AChEI is the most sensitive non-cancer endpoint in multiple species, durations, lifestages, and routes; therefore, it was used as the basis for all selected

endpoints. A dermal absorption factor of 2% (explained in detail in Section 4.2.1) was applied to convert oral doses to dermal equivalent doses to assess risks from dermal exposures.

The toxicology database is complete for human health risk assessment purposes. Endpoints selected for risk assessment are all based on red blood cell (RBC) AChEI from a human volunteer study for all exposure routes except inhalation which used a special acute inhalation study. For infants and young children, a data-derived Food Quality Protection Act (FQPA) Safety Factor (SF) of 2.64X was applied to account for the sensitivity seen in pups in the comparative cholinesterase assay (CCA) since the points of departure (PODs) were derived from studies that only evaluated adults. Section 4.4 addresses the appropriate FQPA SF for oxamyl.

Oxamyl is classified Toxicity Category I for acute oral and Toxicity Category II for acute inhalation. It has low acute toxicity via the dermal routes (Toxicity Category IV). It was found not found to be an eye or dermal irritant (Toxicity Category III and IV), nor a dermal sensitizer.

Residue Chemistry

Provided the labels are revised as indicated in Section 2.3, adequate residue chemistry data are available to support the registered uses. HED is requesting modification to the current tolerance expression and modification to some of the tolerance values (see Section 2.2.2).

Dietary (Food and Water) Exposure and Risk

The acute dietary risk assessment was conducted using the Dietary Exposure Evaluation Model - Food Consumption Intake Database (DEEM-FCID, ver. 3.16) which incorporates food consumption data from the United States Department of Agriculture (USDA) National Health and Nutrition Examination Survey, What We Eat in America (NHANES/WWEIA; 2003-2008). The acute analysis was refined through incorporation of monitoring data from the USDA's Pesticide Data Program (PDP), empirical processing factors, and percent crop treated estimates. For drinking water, modeled surface water estimated drinking water concentrations (EDWCs) derived using the Pesticides in Water Calculator (PWC) were provided by the Environmental Fate and Effects Division (EFED) and the entire distribution was incorporated into the assessment. Groundwater EDWCs were significantly lower than those for surface water and were therefore not incorporated in the analysis. The acute analyses, which are based on AChEI, incorporated a 2.5-hour half-life for recovery of cholinesterase activity by running the assessment using the eating occasion option in DEEM rather than the daily total. The acute (food only) analysis resulted in risk estimates ≤14% of the acute population-adjusted dose (aPAD) (99.9^{th} percentile) for all subpopulations, with children 1-2 years the most highly exposed population subgroup. The commodity-specific analysis (CSA) results in exposure estimates above the level of concern (LOC) for children following consumption of an estimated single serving using PDP monitoring data for one cucumber, one bell pepper, and three summer squash samples. The acute (food and water) analysis resulted in risk estimates that were ≤96% of the aPAD (99.9^{th} percentile) for all subpopulations, with all infants the most highly exposed population. The water only analysis indicate that nearly all of the combined food and water exposures can be attributed to drinking water.

Residential (Non-Occupational) Exposure and Risk

There are currently no registered residential uses of oxamyl; therefore, a residential risk assessment was not conducted.

Spray Drift

A quantitative non-occupational spray drift assessment was conducted for the registered uses of oxamyl. Adult dermal and children's (1 to < 2 years old) dermal and incidental oral risk estimates from indirect exposure related to spray drift are of concern (adult dermal LOC = 10, children's incidental oral and dermal LOC = 26) at a range of distances from the edge of the field (e.g., 0 to >300 feet) depending on the spray-drift scenario. Results indicate that aerial applications result in the highest spray drift risk estimates.

Aggregate

There are no registered residential uses of oxamyl; therefore, the aggregate assessment is equivalent to the dietary (food and drinking water) exposure and risk assessment.

Occupational Exposure and Risk

Occupational handler dermal and inhalation exposure and risk estimates were calculated for the registered uses of oxamyl. Since the toxicological effects are the same (RBC AChEI) but the levels of concern are different (dermal LOC = 10, inhalation LOC = 30), the handler dermal and inhalation exposures are combined using the aggregate risk index (ARI) methodology. The level of concern (LOC) for an ARI is 1 (i.e., ARIs ≥ 1 are not a concern). The occupational handler exposure and risk estimates indicate that the ARIs are of concern (i.e., ARIs are < 1) for many scenarios assuming the use of label-required PPE (double layer of clothing, gloves, a chemical-resistant hat for airblast applications, and a PF10 respirator). Two scenarios (out of 53) do not reach an acceptable ARI with the highest level of mitigation available (i.e., engineering controls).

Occupational post-application dermal exposure and risk estimates were assessed for all registered uses of oxamyl using chemical-specific dislodgeable foliar residue (DFR) data and surrogate cotton boll residue data. Based on the current exposure assessment, dermal post-application MOEs range from 2.4 to 500 on the day of application (LOC = 10). Some scenarios do not reach acceptable MOEs until up to 7 days after application. Both registered product labels currently have REIs of 48 hours.

Based on the Agency's current practices, a quantitative non-cancer occupational post-application inhalation exposure assessment was not performed for oxamyl at this time. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for oxamyl.

Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations[1]."

[1] http://www.archives.gov/federal-register/executive-orders/pdf/12898.pdf

Human Studies Review

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from Pesticide Handlers Exposure Database (PHED) 1.1; the Agricultural Handler Exposure Task Force (AHETF) database; the Outdoor Residential Exposure Task Force (ORETF) database and the Agricultural Reentry Task Force (ARTF) database are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, such as the human volunteer study (MRID 44912301), the ethics review may have included review by the Human Studies Review Board. Descriptions of data sources, as well as guidance on their use, can be found at the Agency website[2].

2.0 HED Conclusions

HED is recommending revisions to the currently registered labels and established tolerances as indicated in Sections 2.3 and 2.2.2, respectively. The dietary and aggregate risk assessment conducted with the DEEM dietary risk estimates are not of concern. The CSA results in exposure estimates above the LOC for children for consumption of individual-size servings using PDP monitoring data for one cucumber, one bell pepper, and three summer squash samples. Some occupational handler risk estimates are of concern to HED (i.e., ARIs <1) when using the labeled PPE (double layer of clothing, gloves, and a PF10 respirator). For two scenarios of concern with label-specified PPE, risks of concern remain even with the highest level of mitigation available (i.e., engineering controls). Occupational post-application MOEs range from 2.4 to 500 on the day of application. Some scenarios do not reach acceptable MOEs until up to 7 days after application (LOC = 10). Both registered product labels (353-532 and 352-372) currently have REIs of 48 hours.

2.1 Data Deficiencies

Provided the labels are revised as indicated in Section 2.3, there were no data deficiencies identified in the toxicological, residue chemistry, or exposure databases.

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

D267628, J. Punzi, 25-JUL-2000

The Food and Drug Administration (FDA) Pesticide Analytical Manual (PAM) Vol. II lists an adequate gas-liquid chromatographic (GLC) method with flame photometric detection (sulfur mode), Method I, for the enforcement of the established/recommended tolerances. This method involves alkaline hydrolysis to convert oxamyl to the oxime metabolite. Therefore, the method determines combined residues of oxamyl and its oxime metabolite.

The FDA PESTDATA database dated 1/94 (PAM Volume I, Appendix I) indicates that oxamyl is completely recovered (>80%) by Multiresidue Methods Section 302 (Luke Method; Protocol D) and Section 401. The registrant has conducted multiresidue methods trials with the oxime

[2] http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data and http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-post-application-exposure

metabolite using Protocols C, D, and E. HED has forwarded the results of these multiresidue trials to FDA for evaluation and inclusion in PAM Vol. I, Appendix I.

2.2.2 Recommended Tolerances

Based on the registered uses, HED concludes that the oxamyl tolerance expression and tolerance values should be revised as indicated below. Note that Table 2.2.2 list only those tolerances where revisions are recommended; for a full list of the recommended and established oxamyl tolerances, see Appendix E.

180.303(a): Tolerances are established for residues of oxamyl, including its metabolites and degradates, in or on the commodities listed in the following table. Compliance with the following tolerance levels is to be determined by measuring the sum of oxamyl (methyl 2-(dimethylamino)-*N*-[[(methylamino)carbonyl]oxy]-2-oxoethanimidothioate) and its oxime metabolite (methyl 2-(dimethylamino)-*N*-hydroxy-2-oxoethanimidothioate), calculated as the stoichiometric equivalent of oxamyl, in or on the following commodities:

Table 2.2.2. Summary of Oxamyl Tolerances.

Commodity	Established Tol. (ppm)	Recommended Tol. (ppm)	Comments
Apple	2	2.0	The tolerance value is being changed to reflect current guidance concerning significant figures.
Banana	0.3	0.30	
Carrot	0.1	0.10	
Celery	10.0	10	
Cotton, undelinted seed	0.2	0.20	
Garlic, bulb	0.2	0.20	
Onion, bulb	0.2	0.20	
Peppermint, tops	10.0	10	
Pineapple	1	1.0	
Spearmint, tops	10.0	10	
Tomato	2	2.0	
Vegetable, tuberous and corm, subgroup 1C	0.1	0.10	
Fruit, citrus, group 10	3		revoke
Fruit, citrus, group 10-10	--	5.0	Updating to 10-10 and harmonizing with the Codex MRL.
Cotton, gin byproducts	--	120	This tolerance was recommended in D372355 (M. Sahafeyan, 29-Jul-2010) but never established.

2.2.3 International Harmonization

Appendix E is a summary of the U.S. tolerances and the Canadian, Codex, and Mexican maximum residue limits (MRLs) for oxamyl. The U.S., Canadian, and Codex tolerance expressions are harmonized. However, Mexico does not include the oxime metabolite in the tolerance expression; therefore, harmonization with the Mexican MRL values is irrelevant. For the commodities where there are U.S., Canadian, and/or Codex tolerances, the tolerance values are harmonized except for the Codex MRLs for citrus and ginger. Based on the available magnitude of the residue data, HED recommends harmonizing the U.S. citrus tolerance level with the Codex MRL (5.0 ppm). However, harmonization with the Codex ginger MRL is not recommended as the value is too low.

2.3 Label Recommendations

Residue Chemistry: Since data concerning the magnitude of the residue in/on the tops of root and tuberous corm vegetables has not been provided and a tolerance is not established in/on crop group 2, the registered labels should be revised to prohibit the harvesting of the tops of root and tuberous corm vegetables (subgroup 1C) for food/feed purposes.

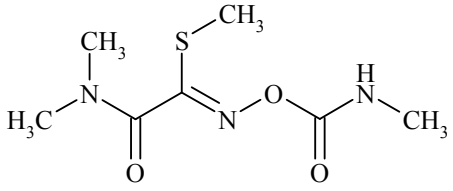
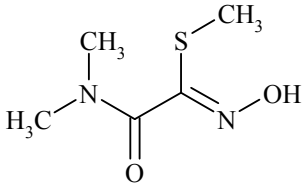
Occupational Exposure: No specific label recommendations are made, however, HED notes that there are several occupational handler and post-application scenarios for registered uses that result in risk estimates of concern. There are also several scenarios that do not reach acceptable post-application MOEs until up to 7 days after application (LOC = 10). The REI on the labels is currently 48 hours.

3.0 Introduction

3.1 Chemical Identity

The chemical structure and nomenclature of oxamyl and its oxime metabolite are summarized in Table 3.1.1. The physicochemical properties of oxamyl are summarized in Appendix B.

Table 3.1.1. Oxamyl and Its Oxime Metabolite Nomenclature.

Chemical structure	
Common name	Oxamyl
Company experimental name	DPX-D1410
IUPAC name	*N*,*N*-dimethyl-2-methylcarbamoyloxyimino-2-(methylthio)acetamide
CAS name	Methyl 2-(dimethylamino)-*N*-[[(methylamino)carbonyl]oxy]-2-oxoethanimidothioate
CAS #	23135-22-0
Chemical structure	
Common Name	Oxime
Company experimental name	DPX-A2213
CAS name	Methyl 2-(dimethylamino)-*N*-hydroxy-2-oxoethanimidothioate
CAS #	66344-33-0

3.2 Pesticide Use Pattern

Oxamyl is registered for use on a variety of agricultural commodities. There are two registered oxamyl Section 3 end-use product labels: DuPont™ Vydate® L (EPA Reg. #352-372) and DuPont™ Vydate® C-LV (EPA Reg. #352-532). Both products are liquid formulations and are RUPs. The labeled use sites include: apples; bananas; cantaloupe; carrots; celery; citrus (orange, lemon, lime, grapefruit); cotton; cucumber; eggplants; garlic; ginger root; honeydew melon; onion (dry bulb); peanuts; pears; peppers; peppermint; pineapples; plantains; potatoes; pumpkin; spearmint; squash; sweet potatoes; tobacco; tomatoes; yams; watermelon; and non-bearing apple, cherry, citrus, peach, and pear. In addition, there are seven Special Local Need (SLN) labels for use of oxamyl on clover grown for seed, onions (dry bulb only), and potatoes in various states. Oxamyl is applied via groundboom sprayer, aerial equipment, airblast sprayer, chemigation, and handheld sprayers. Application rates for oxamyl range from 0.5 to 4 lb ai/acre/day. Oxamyl can be applied from one to eight times a year, depending on the crop. Maximum seasonal application rates range from 2 to 10 lb ai/A. PPE required on the label includes double layer of

clothing, gloves, a chemical-resistant hat for airblast applications, and a PF10 respirator. Both registered product labels currently have REIs of 48 hours. A summary of use site parameters (agricultural and non-agricultural) is listed in Appendix F.

3.3 Anticipated Exposure Pathways

Humans may be exposed to oxamyl in food and drinking water since oxamyl may be applied directly to growing crops and application may result in oxamyl reaching surface and ground water sources of drinking water. There are currently no registered residential uses of oxamyl. Non-occupational exposures may occur as a result of spray drift. In an occupational setting, applicators may be exposed while handling the pesticide prior to application, as well as during application. Occupational post-application exposures may occur when workers enter previously treated agricultural areas. This risk assessment considers all of the aforementioned exposure pathways based on the existing oxamyl uses.

3.4 Consideration of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations[3]." As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the USDA's NHANES/WWEIA and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age and ethnic group. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups, and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures are also evaluated based on home use of pesticide products which includes calculating associated risks for adult applicators and for toddlers, youths, and adults entering or playing in previously treated areas. Spray drift can also potentially result in exposure and it was also considered in this analysis. Further considerations are currently in development, as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

4.0 Hazard Characterization and Dose-Response Assessment

Oxamyl is a member of the NMC class of pesticides. Like other NMCs, the initiating event in the AOP/MOA for oxamyl is inhibition of the enzyme AChE *via* carbamylation of the serine hydroxyl group located in the active site of the enzyme. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system (see Figure 1).

[3] Available: http://www.archives.gov/federal-register/executive-orders/pdf/12898.pdf

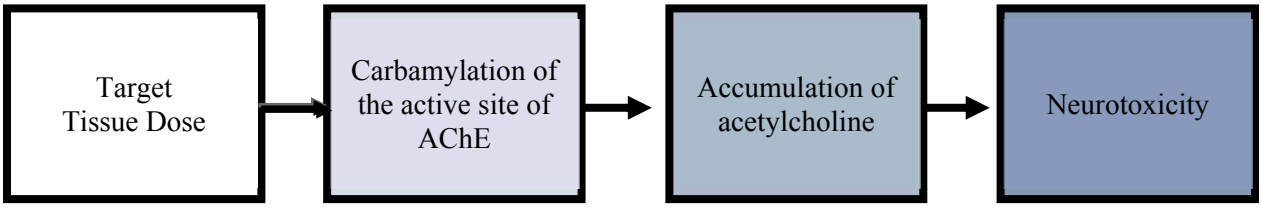


Figure 1. AOP for NMCs.

This MOA is similar to the organophosphate (OP) class of chemicals, as they both result in inhibition of the AChE enzyme. However, they are differentiated by their action upon the active site of the enzyme, which results in clear differences in the timing and duration of inhibition between the two classes. In the OP MOA, inhibition of AChE occurs *via* phosphorylation, which results in an irreversible inhibition of the bound enzyme. Inhibition occurs within a few hours and continues until new, uninhibited enzymes are produced. This results in the OPs exhibiting a phenomenon known as steady-state AChEI. After repeated dosing with an OP at the same dose level, the degree of AChEI comes into equilibrium with the production of new, uninhibited enzyme. At this point, the amount of AChEI at a given dose remains consistent across duration. Therefore, acute and steady-state exposure durations are of concern for OPs.

The NMCs react differently in that carbamylation of the serine hydroxyl group results in a reversible binding process thus allowing for rapid reactivation of the enzyme. The NMCs, therefore, have a unique MOA that results in rapid onset and recovery of the enzyme. The time to peak inhibition for NMCs is typically between 15 to 45 minutes while complete recovery of the enzyme is achieved within minutes to hours[4]. Therefore, for NMCs, including oxamyl, repeated daily exposure does not result in increased inhibition of AChE since enzyme recovery is complete before the next acute exposure, and only acute exposures or a series of acute exposures are a concern for neurotoxic effects.

For oxamyl, AChEI is the most sensitive non-cancer endpoint in the toxicology database in multiple species, durations, lifestages, and routes. NMC specific AChE studies are available that provide information on time to peak inhibition as well as enzyme recovery for oxamyl. AChEI is the focus of the non-cancer hazard characterization; the availability of reliable AChEI dose-response data is one of the key determinants in evaluating the toxicology database.

4.1 Toxicology Studies Available for Analysis

The toxicology database for oxamyl is complete, as described in 40 CFR, Part 158. Based on a weight of evidence approach, the Hazard and Science Policy Council (HASPOC) concluded that an immunotoxicity study is not required at this time for oxamyl (U. Habiba; 18-JUL-2013; TXR# 0056737). Since the RED, human oral (MRID 44912301), CCA (MRID 46615301), AChEI reversibility (44472001), special acute inhalation with AChEI measurements (MRID 45155801), and dermal penetration (MRID 49914101-49914104) studies have been submitted and the results have been incorporated into the current assessment. A benchmark dose (BMD) analysis was conducted on the red blood cell (RBC) and brain AChEI data from the appropriate studies. Appendix A contains a summary of the oxamyl toxicological database. The following toxicology studies have been submitted in support of the registered uses of oxamyl:

(1) Human oral toxicity study;

[4] USEPA (2007). Revised *N*-methyl Carbamate Cumulative Risk Assessment. Office of Pesticide Programs. September 24, 2007.

(2) Subchronic dermal toxicity in rabbits;
(3) Developmental toxicity in rats and rabbits;
(4) Reproductive and postnatal toxicity in rats;
(5) Chronic oral toxicity in rats and dogs;
(6) Carcinogenicity in rats and mice;
(7) Acute and subchronic neurotoxicity in rats;
(8) Genotoxicity studies;
(9) Absorption, distribution, metabolism, and excretion (ADME) studies;
(10) CCA in rats (adults and post-natal day 11 pups);
(11) AChEI reversibility study;
(12) Dermal penetration in rats; and
(13) Special acute inhalation toxicity study in rats with AChEI measurements.

4.2 Absorption, Distribution, Metabolism, and Excretion (ADME)

Following a single oral dose (MRID 41520801), oxamyl is readily absorbed and rapidly metabolized and eliminated in the urine. The major route of excretion is urine, with approximately 80% and 91% of the administered radioactivity eliminated in the urine after 24 hours and 168 hours, respectively. Less than 3% of the dose was found in the feces and approximately 1% was found in the carcass. There were no sex differences and essentially no accumulation of oxamyl or its metabolites in any tissues. The major metabolite of oxamyl in the urine was identified as the β-glucuronide of the oxime (31-37% of dose within 24 hours). The proposed major route of metabolism is through hydrolysis of oxamyl to amine, which is then conjugated with glucuronide.

4.2.1 Dermal Absorption

Triple pack data (rat *in vivo*, rat *in vitro*, and human *in vitro)* are available for two formulations (24% and 42% ai). The highest penetration was observed at the lowest dilution (0.6 g oxamyl/L or 6 µg oxamyl/cm^2) in these studies. Results were similar for both formulations. In the rat *in vivo* studies (MRID 49914102 and 49914104), dermal absorption after 6 hours of exposure at the lowest dilution was 3-5% (sum of excreta, cage wash, carcass, whole blood, residual feed, non-treated skin, stripped skin, and tape strips excluding strips 1-2 observed at 144-hours post-dose). In rat and human skin (MRID 49914101 and 49914103), 5-6% and 1-2% was absorbed into the receptor fluid, respectively, at the lowest dilution. A refined dermal absorption factor (DAF) of 2% was calculated from the results obtained from these dermal penetrations studies (refined DAF = rat *in vivo* x human *in vitro* ÷ rat *in vitro* = 5% x 2% ÷ 6% = 2%) and is used in the current assessment for converting oral doses to dermal equivalent doses to assess the potential risk associated with dermal exposures of oxamyl (see Section 4.5.1).

4.3 Toxicological Effects

The nervous system is the primary target for oxamyl and AChEI is the most sensitive endpoint in multiple species, durations, lifestages, and routes. Oral, dermal, and inhalation studies that evaluate AChEI are available for oxamyl. Inhibition has been shown to be rapid, but also reversible within hours. Therefore, for oxamyl, repeated daily exposure does not result in increased inhibition of AChE since enzyme recovery is complete before the next acute exposure. Therefore, acute exposures or a series of acute exposures are the main exposure duration of concern for oxamyl neurotoxicity.

Data are available describing the time to peak AChEI and dose-response of oxamyl brain and RBC AChEI. A human *in vivo* volunteer study (MRID 44912301) was evaluated by the Human Studies Review Board and determined to be ethically and scientifically valid for use in risk assessment[5]. In this study, RBC AChEI occurred at doses >0.06 mg/kg (BMD_{10} = 0.083 mg/kg; $BMDL_{10}$ = 0.069 mg/kg) with RBC peak inhibition within 45-60 minutes and recovery 3-4 hours post-dosing. The CCA study in rats found that peak inhibition occurs within 30 minutes for adult and post-natal day (PND) 11 pups (MRID 46615301). Estimates of recovery half-lives in the CCA demonstrate that recovery is slightly longer in the PND11 pups (RBC = 2.5 hours, brain = 1.34 hours) as compared to adult rats (RBC = 0.76 hours, brain = 0.62 hours). The human adult recovery half-life estimate for RBC (2.37 hours) is similar to that of the PND11 pups.

The CCA study also provided a direct comparison of the magnitude of AChEI in the PND11 pups to adult animals. The data demonstrate that PND11 pups are more sensitive to oxamyl than adult rats, particularly in the brain (0.177/0.067 = 2.64X) (Table 4.3). A comparison of central estimates (BMD_{10}) indicates that there is little difference in compartment sensitivity in the young (0.067/0.059 = 1.14X). For adults, however, the data indicate that RBCs are the more sensitive compartment.

Table 4.3. Comparative Cholinesterase Study Results (MRID 46615301).

	Brain (mg/kg)		RBC (mg/kg)	
Age	**BMD_{10}**	**$BMDL_{10}$**	**BMD_{10}**	**$BMDL_{10}$**
PND11 pups	0.067	0.043	0.059	0.039
Adults	0.177	0.145	0.079	0.052

Apparent quantitative susceptibility was noted in the rat developmental toxicity study where decreased fetal bodyweights were observed; however, this occurred at a dose well above the BMD_{10} for PND11 pups and adult animals in the CCA study. There was no evidence of increased susceptibility in the rabbit developmental or reproduction toxicity studies.

In the rat acute and subchronic neurotoxicity studies, clinical signs of neurotoxicity (e.g., tremors, salivation, abnormal gait, low posture, hyperactivity), numerous effects in the functional observation battery (e.g., decreased grip strength, impaired locomotion, lacrimation, dilated pupils, piloerection), and decreased motor activity were seen at doses that resulted in significant AChEI (>30%). Similar signs were observed in other studies across the toxicological database for oxamyl.

Route-specific dermal and inhalation toxicity studies are available for oxamyl. There are two dermal toxicity studies available in rabbits; however, one study (MRID 44751201) has been classified as unacceptable. In the acceptable study (MRID 40827601), AChEI was observed with a BMD_{10} of 23.1 mg/kg/day ($BMDL_{10}$ = 8 mg/kg/day) in RBC and a BMD_{10} of 20.2 mg/kg/day ($BMDL_{10}$ = 15.9 mg/kg/day) in the brain. In the special acute inhalation study (MRID 45155801), AChEI was similar in the brain (BMD_{10} = 0.005 mg/L) and RBC (BMD_{10} = 0.002 mg/L). At the highest concentration tested (0.024 mg/L), clinical signs of neurotoxicity (tremors and lethargy) were observed. No histopathological evaluations were performed in this study.

Oxamyl is classified Toxicity Category I for acute oral, and Toxicity Category II for acute inhalation. It has low acute toxicity via the dermal routes (Toxicity Category IV). It was found not found to be an eye or dermal irritant (Toxicity Category III and IV), nor a dermal sensitizer.

[5] https://archive.epa.gov/osa/hsrb/web/pdf/april2006mtgteleconfreport51606-2.pdf

4.4 Safety Factor for Infants and Children (FQPA Safety Factor)[6]

As previously described, the Agency has a non-guideline CCA study in the rat that directly compares the magnitude of AChEI in the young (PND 11 pups) to the magnitude of AChEI in adults. Based on the results of this study, the Agency concluded that pups were more sensitive to oxamyl than adult rats, particularly in the brain. Since adult data were used to derive PODs, a data derived FQPA SF of 2.64X will be applied for exposure scenarios for infants and young children (< 6 years old).

4.4.1 Completeness of the Toxicology Database

The existing toxicological database is adequate for FQPA evaluation and evaluates all relevant lifestages. The rat CCA, rat and rabbit developmental toxicity, rat reproduction, and neurotoxicity (acute and subchronic) studies are available for FQPA consideration.

4.4.2 Evidence of Neurotoxicity

Oxamyl is a member of the common mechanism group known as the NMCs. As with other NMCs, oxamyl causes neurotoxicity through the inhibition of AChE leading to clinical signs of neurotoxicity (see Section 4.3). The most sensitive effect in all species, routes, and lifestages is AChEI, which is used for deriving all PODs and is protective of the clinical signs observed in the database.

4.4.3 Evidence of Sensitivity/Susceptibility in the Developing or Young Animal

There was evidence of increased quantitative susceptibility in rat developmental and CCA studies (see section 4.3). Since there are multiple studies for oxamyl with appropriate AChE data for both brain and RBC, there are several options for endpoint selection. A comparison of the AChE data and appropriate uncertainty factors, including the data used in the Revised NMC cumulative risk assessment (CRA), was performed (E. Reaves; 01-JUL-2010; D379814; TXR# 0055406). Although the FQPA factor is typically derived from the same compartment as that relied upon for the POD, in this data set, the Agency does not have brain AChE data from humans, only RBC AChE data. Therefore, since the PND11 rat pups were more sensitive than adult rats in the CCA study, particularly in the brain, the brain FQPA SF from the rodent data would be protective of the brain compartment in humans. Based on this weight of evidence approach, the most appropriate FQPA SF to be applied for exposure scenarios for infants and young children (< 6 years old) is a data derived FQPA SF of 2.64X based on the comparison of brain data in adult rodents and PND11 pups from the CCA study (Table 4.4.3). Additional information regarding the selection of this FQPA SF can be found in the updated toxicity endpoints memo (E. Reaves; 01-JUL-2010; D379814; TXR# 0055406).

Table 4.4.3. FQPA SF Based on AChEI in the Oxamyl CCA Study.

Compartment	Adult BMD_{10}[1]	PND 11 Pups BMD_{10}	FQPA SF[2]
Brain	0.177	0.067	2.64

[1] BMD_{10} is defined as the estimated dose at which 10% AChEI would be observed.
[2] The FQPA SF is calculated by dividing the BMD_{10} for the adults by the BMD_{10} of the pups for the same sex and compartment.

[6] HED's standard toxicological, exposure, and risk assessment approaches are consistent with the requirements of EPA's children's environmental health policy (https://www.epa.gov/children/epas-policy-evaluating-risk-children).

4.4.4 Residual Uncertainty in the Exposure Database

The exposure databases are sufficient to determine the nature/magnitude of the residue in food. The dietary exposure analyses are unlikely to underestimate exposure as they incorporated robust monitoring data and modeled drinking water estimates. The non-occupational assessments are based upon the 2012 Standard Operating Procedures (SOPs) for Residential Pesticide Exposure Assessment. These assessments of exposure are not likely to underestimate the resulting estimates of risk from exposure to oxamyl.

4.5 Toxicology Endpoint and Point of Departure Selections

Table 4.5.4.1 and 4.5.4.2 summarize the toxicological doses and endpoints selected for dietary, non-occupational, and occupational risk assessments. The rationale for the dose/endpoint selection is also described below. The endpoints were updated in 2010 (E. Reaves; 01-JUL-2010; D379814; TXR# 0055406) and there have been no changes to the previously selected endpoints except the dermal endpoint. Additionally, an incidental oral endpoint was selected for evaluating potential exposure from spray drift and the inhalation calculations have been updated using current practices. All endpoints are based on the BMD_{10}, which is the dose estimated to produce 10% inhibition of AChE compared to background. Only acute exposures or a series of acute exposures are of concern for oxamyl because repeated daily exposures do not result in increased inhibition of AChE due to complete enzyme recovery before the next acute exposure. As a result, the same endpoint is selected for all durations of an exposure route and short-term assessments are considered protective of intermediate-term assessments. There are no long-term exposures expected for oxamyl.

4.5.1 Dose-Response Assessment

As discussed previously, peak inhibition of AChE occurs rapidly (within 30-60 minutes after dosing in the human oral study; 30 minutes for juvenile and adult rats) with recovery occurring within minutes to hours (estimated recovery half-life for PND11 pups is 2.5 hours, which is similar to the 2.4-hour recovery half-life observed in the human oral study). In addition, the toxicological database for oxamyl indicates that the magnitude of AChEI does not increase with repeated exposures; therefore, acute exposure is the duration of concern for neurotoxicity. There are no chronic effects more sensitive than AChEI.

Consistent with risk assessments for other AChE-inhibiting compounds, OPP has used a benchmark response (BMR) level of 10% and calculated BMD_{10} and $BMDL_{10}$ values. The BMD_{10} is the estimated dose where AChE is inhibited by 10% compared to background. The $BMDL_{10}$ is the lower confidence bound on the BMD_{10}. As a matter of science policy, the Agency uses the BMDL, not the BMD, for the POD[7].

Acute Dietary (All Populations): The human oral study which demonstrated enzyme inhibition within minutes and recovery within minutes to hours following a single dose was selected to evaluate acute dietary exposures. This study is supported by the weight of evidence available for AChE data (rodent and human) for oxamyl. A $BMDL_{10}$ of 0.069 mg/kg (BMD_{10} = 0.083 mg/kg) was derived based on inhibition of RBC AChE activity. This study is appropriate for the oral

[7] U.S. EPA. 2012. Benchmark Dose Technical Guidance. Riks Assessment Forum, U.S. Environmental Protection Agency, Washington, DC.

route and duration of exposure. Since a human study was selected to evaluate acute dietary exposures, the interspecies extrapolation factor has been reduced to 1X. For all subpopulations, except infants and children, the aPAD of 0.0069 mg/kg is based on the $BMDL_{10}$ of 0.069 mg/kg and a 10X total uncertainty factor (1X for interspecies extrapolation, 10X for intraspecies extrapolation, and 1X for FQPA SF). The study was conducted in adults only; therefore, the FQPA SF will be applied when assessing acute dietary exposure for infants and children. As a result, the aPAD for infants and children is 0.0026 mg/kg based on the $BMDL_{10}$ of 0.069 mg/kg and a 26-fold uncertainty factor (1X for interspecies extrapolation, 10X for intraspecies extrapolation, and 2.64X for FQPA SF). A 2.5-hour recovery half-life estimate is applicable for all populations based on PND11 rats in the CCA study and supported by the recovery half-life observed in the human oral study (2.4 hours).

Chronic Dietary (All Populations): A chronic dietary assessment was not conducted since recovery data demonstrate that there is rapid recovery of AChE following acute exposure to oxamyl, which prevents cumulative toxicity. Consequently, longer-term exposures are considered to be equivalent to a series of acute exposures. Therefore, a chronic assessment is not considered appropriate for oxamyl.

Short- and Intermediate-Term Incidental Oral: The human oral study was selected to evaluate incidental oral exposures since it is appropriate for the route and duration of exposure. Short- and intermediate-term exposures can be considered as a series of acute exposures, with regard to AChEI. A $BMDL_{10}$ of 0.069 mg/kg (BMD_{10} = 0.083 mg/kg) was derived based on inhibition of RBC AChE activity. Since a human study was selected to evaluate incidental oral exposures, the interspecies extrapolation factor may be reduced to 1X. The study was conducted in adults only; therefore, the FQPA SF will be applied when assessing incidental oral exposures for infants and children. Therefore, the LOC for incidental oral exposures is 26 (1X for interspecies extrapolation, 10X for intraspecies extrapolation, and 2.64X for FQPA SF).

Short- and Intermediate-Term Dermal: For the last endpoint update (E. Reaves; 01-JUL-2010; D379814; TXR# 0055406), a route-specific study in rabbits (MRID 40827601) was selected to evaluate dermal exposures. This study was considered for the current assessment; however, the human oral study was also considered along with the recently submitted triple pack dermal penetration data (*in vivo* rat dermal penetration studies and *in vitro* dermal penetrations studies with human and rat skin) allowing for the derivation of a refined DAF. Given the availability of species-specific data in humans for this human health risk assessment, the human oral study was selected to evaluate dermal exposures with a $BMDL_{10}$ of 0.069 mg/kg (BMD_{10} = 0.083 mg/kg) based on inhibition of RBC AChE activity. A refined DAF of 2% from the dermal penetration triple pack studies may be applied to convert oral doses to dermal equivalent doses to assess risks from dermal exposures (see Section 4.2.1). Since a human study was selected to evaluate dermal exposures, the interspecies extrapolation factor may be reduced to 1X. For all populations, except infants and children, the LOC for dermal exposures is 10 (1X for interspecies extrapolation, 10X for intraspecies extrapolation, and 1X for FQPA SF). The study was conducted in adults only; therefore, the FQPA SF will be applied when assessing dermal exposures for infants and children resulting in a LOC of 26 (1X for interspecies extrapolation, 10X for intraspecies extrapolation, and 2.64X for FQPA SF).

Short- and Intermediate-Term Inhalation: There is a special acute inhalation toxicity study in rats available for oxamyl with AChEI measurements. A BMD_{10} of 0.002 mg/L ($BMDL_{10}$ = 0.0018 mg/L) was derived based on inhibition of RBC AChE activity in both sexes. This study is appropriate for the route and duration of exposure. Unlike dermal exposures, the amount of

absorption via the inhalation route is unknown; therefore, the human oral study was not selected to evaluate inhalation exposures; however, it was noted that use of the human oral study would not change the overall risk assessment conclusions. Human-equivalent concentrations and doses were calculated using the $BMDL_{10}$ and the regional deposited-dose ratio (RDDR) based on the special acute inhalation study. The RDDR accounts for the particulate diameter [mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD)] and estimates the different dose fractions deposited along the respiratory tract. The RDDR also accounts for interspecies differences in ventilation and respiratory tract surface areas. For the special acute inhalation study, a systemic RDDR was estimated at 2.49 based on extrarespiratory effects, a MMAD of 0.85 µm, and GSD of 2.3 µm from the lowest dose tested (0.0049 mg/L).

The POD from the route-specific inhalation study was adjusted for expected human exposure duration. Duration adjustment is performed based on Haber's law, which assumes that a toxicological effect is proportional to the product of exposure level and duration. Animal-to-human ratios of daily (hours/day) and weekly (days/week) exposures may be applied to the animal inhalation study POD when the expected duration of the exposure scenario is longer than the duration in the available inhalation toxicity study. In the case of oxamyl, a daily duration adjustment (from 4 hours/day exposure in the acute rat inhalation study) was applied when appropriate; however, no weekly adjustment was made since the study only evaluated acute (1 day) exposure. The RDDR of 2.49 was applied to the duration-adjusted POD to obtain human equivalent concentrations, which were then used to calculate subsequent human equivalent doses[8]. The resulting human equivalent concentrations and doses are presented in Table 4.5.4.3.

The standard interspecies extrapolation uncertainty factor can be reduced from 10X to 3X due to the calculation of human equivalent concentrations accounting for pharmacokinetic (not pharmacodynamics) interspecies differences. As a result, the LOC for inhalation exposures for adults is 30 (3X for interspecies extrapolation, 10X for intraspecies sensitivity, and 1X for FQPA SF when applicable). For infants and children (< 6 years old), the FQPA SF would need to be applied resulting in a LOC of 79 (3X for interspecies extrapolation, 10X for intraspecies sensitivity, and 2.64X for FQPA SF).

4.5.2 Recommendations for Combining Routes of Exposure for Risk Assessment

For all durations, oral, dermal, and inhalation exposures can be combined since the same effect (i.e., RBC AChEI) was observed in the selected endpoints for risk assessment.

4.5.3 Cancer Classification and Risk Assessment Recommendation

Oxamyl is classified as a Group E (evidence of non-carcinogenicity for humans) chemical based on lack of evidence of carcinogenicity in rats and mice (R. Whiting; 5-NOV-1996; TXR# 0051137).

[8] Human equivalent dose (mg/kg/day) = human equivalent concentration (mg/L) x human-specific conversion factor (11.8 L/hr-kg) x respiratory tract to oral absorption ratio (assume 1) x duration of daily exposure for activity (occupational handler = 8 hrs/day, residential handler and indoor post-application = 2 hrs/day, residential outdoor post-application = 2.3 hrs/day)

4.5.4 Summary of Points of Departure and Toxicity Endpoints Used in Human Risk Assessment

Table 4.5.4.1. Summary of Toxicological Doses and Endpoints for Oxamyl for Use in Dietary and Non-Occupational Human Health Risk Assessments.

Exposure/ Scenario	POD	Uncertainty/FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (All populations except infants and young children)	$BMDL_{10}$ = 0.069 mg/kg	UF_A = 1X UF_H = 10X FQPA SF = 1X	aRfD = aPAD = 0.0069 mg/kg/day (recovery half-life = 2.5 hours)	Human Oral Study (MRID 44912301) BMD_{10} = 0.083 mg/kg based on RBC AChEI
Acute Dietary (Infants and young children)	$BMDL_{10}$ = 0.069 mg/kg	UF_A = 1X UF_H =10X FQPA SF = 2.64X$^+$	aRfD = 0.0069 mg/kg/day aPAD = 0.0026 mg/kg/day (recovery half-life = 2.5 hours)	Human Oral Study (MRID 44912301) BMD_{10} = 0.083 mg/kg based on RBC AChEI
Chronic Dietary (All Populations)	Since the peak AChEI occurs quickly and recovers within hours, repeated daily exposure does not result in increased inhibition of AChE as the enzyme recovery is complete before the next acute exposure. Therefore, only acute exposure durations are of concern for oxamyl.			
Incidental Oral Short-term (1-30days) and Intermediate-term (1-6 months) Infants and young children	$BMDL_{10}$ = 0.069 mg/kg	UF_A = 1X UF_H =10X FQPA SF = 2.64X$^+$	Residential LOC for MOEs <26	Human Oral Study (MRID 44912301) BMD_{10} = 0.083 mg/kg based on RBC AChEI
Dermal Short-(1-30 days) and intermediate-terms (1-6 months) Infants and young children	$BMDL_{10}$ = 0.069 mg/kg DAF = 2%[1]	UF_A = 1X UF_H =10X FQPA SF = 2.64X$^+$	Residential LOC for MOEs <26	Human Oral Study (MRID 44912301) BMD_{10} = 0.083 mg/kg based on RBC AChEI
Dermal Short-(1-30 days) and intermediate-terms (1-6 months) Adults	$BMDL_{10}$ = 0.069 mg/kg DAF = 2%[1]	UF_A = 1X UF_H =10X FQPA SF = 1X	Residential LOC for MOEs <10	Human Oral Study (MRID 44912301) BMD_{10} = 0.083 mg/kg based on RBC AChEI
Inhalation Short-(1-30 days) & intermediate (1-6 months) Infants and young children	$BMDL_{10}$ = 0.0018 mg/L	UF_A = 3X UF_H =10X FQPA SF = 2.64X$^+$	Residential LOC for MOEs <79	Acute Rat Inhalation Study (MRID 45155801) BMD_{10} = 0.02 mg/L based on RBC AChEI in both sexes
Inhalation Short-(1-30 days) & intermediate (1-6 months) Adults	$BMDL_{10}$ = 0.0018 mg/L	UF_A = 3X UF_H =10X FQPA SF = 1X	Residential LOC for MOEs <30	Acute Rat Inhalation Study (MRID 45155801) BMD_{10} = 0.002 mg/L based on RBC AChEI in both sexes

Table 4.5.4.1. Summary of Toxicological Doses and Endpoints for Oxamyl for Use in Dietary and Non-Occupational Human Health Risk Assessments.				
Exposure/ Scenario	**POD**	**Uncertainty/FQPA Safety Factors**	**RfD, PAD, Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Cancer (oral, dermal, inhalation)	Classified as Group E (evidence of non-carcinogenicity for humans).			

Point of departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no-observed adverse-effect level. LOAEL = lowest-observed adverse-effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). PAD = population-adjusted dose (c = chronic). RfD = reference dose. LOC = level of concern. BMD = bench mark dose. FQPA SF = FQPA Safety Factor. DAF = dermal absorption factor.
[+]FQPA safety factor calculated at 2.64X (E. Reaves; 1-JUL-2010; D379814).
[1] DAF = 2% based on triple pack data (rat *in vivo* x human *in vitro* ÷ rat *in vitro* = 5% x 2% ÷ 6% = 2%).

Table 4.5.4.2. Summary of Toxicological Doses and Endpoints for Oxamyl for Use in Occupational Human Health Risk Assessments.				
Exposure/ Scenario	**POD**	**Uncertainty/FQPA Safety Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Dermal Short-(1-30 days) and intermediate-terms (1-6 months) Adults	$BMDL_{10}$ = 0.069 mg/kg DAF = 2%[1]	UF_A = 1X UF_H = 10X	Occupational LOC for MOEs <10	Human Oral Study (MRID 44912301) BMD_{10} = 0.083 mg/kg based on RBC AChEI
Inhalation Short-(1-30 days) & intermediate (1-6 months) Adults	$BMDL_{10}$ = 0.0018 mg/L	UF_A= 3X UF_H = 10X	Occupational LOC for MOEs <30	Acute Rat Inhalation Study (MRID 45155801) BMD_{10} = 0.02 mg/L based on RBC AChEI in both sexes
Cancer (oral, dermal, inhalation)	Classified as Group E (evidence of non-carcinogenicity for humans).			

Point of departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no-observed adverse-effect level. LOAEL = lowest-observed adverse-effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). PAD = population-adjusted dose (c = chronic). RfD = reference dose. LOC = level of concern. BMD = bench mark dose. FQPA SF = FQPA Safety Factor.
[+]FQPA safety factor calculated at 2.64X (E. Reaves; 1-JUL-2010; D379814).
DAF = 2% based on triple pack data (rat *in vivo* x human *in vitro* ÷ rat *in vitro* = 5% x 2% ÷ 6% = 2%).

Table 4.5.4.3. Calculated Inhalation Human-Equivalent Concentrations and Doses for Oxamyl.						
Population	**Scenario**	**Duration adjustment[a]**		**Human equivalent concentration[b]**		**Human equivalent dose (mg/kg/day)**
		hr/day	**day/wk**	**mg/L**	**mg/m3**	
Occupational	Handler	8	NA	0.002	2.241	0.212
Residential	Handler	NA	NA	0.004	4.482	0.106
	Outdoor post-application	NA	NA	0.004	4.482	0.122
	Indoor Post-application	NA	NA	0.004	4.482	0.106
	Bystander	24	NA	0.001	0.747	--

a. Toxicity duration adjustment from 4 hours/day exposure in the acute rat inhalation study (MRID 45155801). No weekly adjustment was made since the study only evaluated acute (1 day) exposure.
b. Human equivalent concentrations calculated using duration adjustments, when applicable, and a systemic regional deposited dose ratio (RDDR) of 2.49, which was obtained with a mass median aerodynamic diameter (MMAD) of 0.85 µm and a geometric

standard deviation (GSD) of 2.3 µm from the lowest dose tested (0.0049 mg/L), as well as the combined sex body weight of 178 g from the acute rat inhalation study (MRID 45155801).
NA = not applicable (the expected duration of the exposure scenario is less than the duration in the available inhalation toxicity studies; downward adjustments are not permitted).

4.6 Endocrine Disruption

As required by Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and Federal Food, Drug and Cosmetic Act (FFDCA), EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of the reregistration decision for oxamyl, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), oxamyl is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[9] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.

Oxamyl is on List 1 for which EPA has received all of the required Tier 1 assay data. The Agency has reviewed all of the assay data received for the appropriate List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets (see EPA-HQ-OPP-2010-0028 for oxamyl). For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website[10].

[9] See http://www.epa.gov/endocrine-disruption/overview-second-list-chemicals-tier-1-screening-under-endocrine-disruptor for the final second list of chemicals.
[10] http://www.epa.gov/endo/

5.0 Dietary Exposure and Risk Assessment

Oxamyl Registration Standard, C. Trichilo, 30-JAN-1987; D209731, L. Cheng, 25-JUN-1996; D260911, J. Punzi, 5-JAN-2000; D267628, J. Punzi, 25-JUL-2000; D372355, M. Sahafeyan, 29-JUL-2010; D368180, C. Smith *et al.*, 18-Aug-2010

5.1 Metabolite/Degradate Residue Profile

5.1.1 Summary of Plant and Animal Metabolism Studies

Primary Crops: The qualitative nature of the residue in plants is adequately understood based on metabolism studies conducted with alfalfa, apples, beans, cotton, oranges, peanuts, potatoes, tobacco, and tomatoes. Oxamyl was found to undergo hydrolysis of the methylcarbamoyl group to the oxime metabolite which then conjugates to form a glucoside. The oxime glucoside may undergo demethylation to form oximino methyl glucoside, and both glucosides may be incorporated into plant polysaccharides.

Ruminants: The qualitative nature of the residue in livestock is adequately understood based on metabolism studies conducted with lactating goats (dietary burden = 31 ppm; 18x; see Appendix D for dietary burden calculations) and laying hens (dietary burden = 30 ppm; 600x). Oxamyl was found to be rapidly and extensively metabolized in both lactating goats and laying hens. Thiocyanate was a major metabolite in milk (32-49%), egg (23-33%), and tissues (3-35%). Also identified in goat liver were *N*-methyloxamic acid/*N*-methyloxamide (15-20% TRR) and oxalic acid (17% TRR). Oxamyl was not identified in any matrix nor were the following compounds: oxamyl sulfone, oxamyl sulfoxide, oxime, oxime sulfoxide, oxime sulfone, *N*-methyloxime, and *N*-dimethylcyanoformamide. Based on these data and the livestock dietary burdens (see Appendix D), HED has concluded that residues in livestock are likely to be insignificant (180.6(a)(2)) and livestock feeding studies are unnecessary (D209731, L. Cheng, 25-JUN-1996; D372355, M. Sahafeyan, 29-JUL-2010).

Rotational Crops: Data from adequate confined and field rotational crop studies, in conjunction with the plant metabolism profile, indicate that rotational crop tolerances are not needed provided the seasonal application rate does not exceed 12 lbs ai/acre and a 4-month plant-back interval (PBI) is established. The registered labels specify maximum seasonal rates of <12 lbs ai/acre and a 4-month PBI.

5.1.2 Summary of Environmental Degradation

Oxamyl is hydrophilic, mobile to highly mobile in soil, and relatively nonvolatile. The compound dissipates in the environment by chemical (abiotic) and microbially-influenced (biotic) degradation and by leaching. Degradation half-lives are on the order of days in most soils and in neutral pH water bodies. However, oxamyl persists for weeks in some soils and may persist for months to years in some aerobic, acidic, and saturated sub-soils (oxamyl is slow to hydrolyze in acidic environments).

Major degradates of oxamyl include the oxime, DMOA, DMCF, DMEA, and carbon dioxide (see Appendix C for names structures); none of these contain the NMC moiety of the parent compound. Oxamyl may leach to ground water or move to surface water bodies through spray drift and/or dissolved in runoff. The compound is not expected to bioaccumulate in aquatic or terrestrial organisms.

5.1.3 Comparison of Metabolic Pathways

In rats, the major metabolite of oxamyl was the β-glucuronide of the oxime. The proposed major route of metabolism is through hydrolysis of oxamyl to amine, which is then conjugated with glucuronide. In plants, oxamyl was found to undergo hydrolysis of the methylcarbamoyl group to form the oxime metabolite which then conjugates to form a glucoside. The oxime glucoside may undergo demethylation to form oximino methyl glucoside, and both glucosides may be incorporated into plant polysaccharides. In the environment, oxamyl was also found to degrade to oxime which is then further degraded to DMOA, DMCF, and/or DMEA. Based on the current registrations and the available data, residues in livestock are expected to be negligible.

5.1.4 Residues of Concern Summary

Based on the information summarized above and toxicological considerations, the residues of concern in crops (primary and rotational), livestock, and drinking water are as defined in Table 5.1.4. The oxime metabolite was included as a residue of concern for purposes of tolerance expression in primary crops as the submitted residue data employed a method which converted parent to oxime. Oxime is not included in the risk assessment as it is not likely to be a potent acetyl cholinesterase inhibitor. In addition, it was concluded that exposure to thiocyanate (a major metabolite in milk, egg, and livestock tissues) from oxamyl will be negligible as compared to the background exposure to thiocyanate through normal human metabolic processes and consumption of foods which naturally contain thiocyanate (D260911, J. Punzi, 5-JAN-2000).

Table 5.1.4. Summary of ROCs for Risk Assessment and Tolerance Enforcement.

Matrix		Residues Included in Risk Assessment	Residues Included in Tolerance Expression
Plants	Primary Crop	oxamyl	oxamyl and oxime
	Rotational Crop	Rotational crop tolerances are not needed provided the application rate does not exceed 12 lbs ai/acre and a 4-month plant-back interval (PBI) is established.	
Livestock	Ruminant	not determined; 40 CFR 180.6(a)(3)[1]	
	Poultry		
Drinking Water		oxamyl	not applicable

[1] D209731, L. Cheng, 25-JUN-1996; D372355, M. Sahafeyan, 29-JUL-2010.

5.2 Food Residue Profile

Adequate field trial and processing data have been submitted to support all of the currently registered uses. The samples were analyzed using an adequately validated analytical method and the storage intervals were also validated. In addition, HED has concluded that based on the results of the livestock metabolism studies and the livestock dietary burdens, there is no reasonable expectation of finite oxamyl residues in livestock commodities (40 CFR 180.6(a)(3); feeding studies are unnecessary; D372355, M. Sahafeyan, 29-JUL-2010; D209731, L. Cheng, 25-JUN-1996). No additional residue chemistry data are needed to support the currently registered uses. HED notes that a cotton gin byproducts tolerance at 120 ppm should be established as recommended in D372355 (M. Sahafeyan, 29-JUL-2010). In addition, since oxamyl is only registered for application to ginger, potato, sweet potato, and yam, HED is recommending deletion of the subgroup 1C tolerance and establishment of individual tolerances in/on the aforementioned crops. Finally, since data concerning the magnitude of the residue in sweet potato tops (member of crop group 2) has not been provided and a tolerance has not been

established, the registered labels should be revised to prohibit the harvesting of sweet potato leaves for food/feed purposes.

5.3 Water Residue Profile

The residue of concern in drinking water is parent oxamyl only. EFED recently provided EDWCs with the scenarios recommended for inclusion in the dietary assessment (D438940, F. Khan, 9-May-2017). A summary of the scenarios resulting in the highest drinking water estimates are presented in Table 5.3, with applications to melons providing the worst case EDWCs. As a result, the entire surface water distribution resulting from application to melons was incorporated into the dietary assessment. EFED previously provided Tier 1 EDWCs resulting from application of oxamyl to ginger, pineapple, and yams which are significantly higher than those summarized in Table 5.3 (D372628, G. Orrick, 17-Feb-2010; FIRST model). Tier 2 model scenarios are not available for these crops. Although the Tier 1 estimates for ginger, pineapple, and yam were not included in the dietary assessment, it is noted that the application rates for these crops are less than the application rates modeled for melon and tomato.

Table 5.3. EDWCs.

Drinking Water Source	Modeled Rate[1]	1-in-10 Year Peak (µg/L)	1-in-10-Year Annual Mean (µg/L)	30-Year Mean (µg/L)
surface water (PWC)	melon (12 x 1.0 lb ai/acre)	77.7	2.6	1.5
	tomato (16 x 1.0 lb ai/acre)	55.5	2.0	0.94
groundwater (PRZM-GW)	tomato (16 x 1.0 lb ai/acre)	Peak (µg/L)	Post-Breakthrough Average (µg/L)	
		16	0.03	

[1] Assumes multiple crop seasons per year.

5.4 Dietary Risk Assessment

D439440, T. Bloem, 31-May-2017

5.4.1 Overview of Residue Data Used

The dietary analysis included percent crop treated information, empirical processing data (when available), and monitoring data from the USDA PDP. For drinking water, the acute assessments incorporated the entire surface water distributions resulting from application to melons as it provided the worst case EDWCs.

5.4.2 Percent Crop Treated Used in Dietary Assessment

The acute assessment included screening level usage analysis (SLUA) data provided by the Biological Economic Analysis Division (BEAD; 7-JUN-2016). The following maximum percent crop treated estimates were incorporated into the acute analysis: apple (<2.5%), cantaloupe (15%), carrot (10%), celery (55%), cotton (5%), cucumber (20%), garlic (15%), grapefruit (15%), onion (30%), orange (5%), peanut (<2.5%), pepper (40%), potato (25%), pumpkin (5%), squash (25%), tomato (10%), and watermelon (15%).

5.4.3 Acute Dietary Risk Assessment

The acute (food and drinking water) analysis incorporating the surface water distributions from application to melons results in risk estimates ≤96% aPAD, at the 99.9th percentile of exposure,

for all subpopulations, with all infants as the most highly exposed population (Table 5.4.3). A water only analysis indicates that nearly all of the dietary exposures can be attributed to drinking water. A food-only analysis resulted in risk estimates ≤14% aPAD for all subpopulations, with children 1-2 years old the most highly exposed population. The majority of the food only exposure estimates for all populations derived from summer squash (14-54% of total exposure), cucumber (7-44% of total exposure), watermelon (<1-13% of total exposure), nonbell peppers (<1-22% of total exposure), bell peppers (<1-20% of total exposure), and carrots (<1-5% of total exposure).

Table 5.4.3. Results of Acute Dietary Exposure and Risk Analysis (eating occasion; half-life = 2.5 hours).

Population Subgroup[1]	aPAD (mg/kg/day)	95th Percentile		99th Percentile		99.9th Percentile[1]	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	%aPAD
Food Only							
general U.S. Population	0.0069 (0.0026 for children <6 years old)	0.000026	<1	0.000059	<1	0.000178	2.6
all Infants (<1 year old)		0.000064	2.5	0.000105	4.0	0.000184	7.1
children 1-2 years old		0.000066	2.6	0.000138	5.3	**0.000356**	**14**
children 3-5 years old		0.000055	2.1	0.000102	3.9	0.000312	12
children 6-12 years old		0.000035	<1	0.000069	1.0	0.000200	2.9
youth 13-19 years old		0.000020	<1	0.000044	<1	0.000132	1.9
adults 20-49 years old		0.000019	<1	0.000046	<1	0.000166	2.4
adults 50-99 years old		0.000017	<1	0.000037	<1	0.000150	2.2
females 13-49 years old		0.000019	<1	0.000046	<1	0.000170	2.5
Food and drinking water (surface drinking water estimates based on application to melons; water only in parenthesis)							
general U.S. Population	0.0069 (0.0026 for children <6 years old)	0.000078	1.1	0.000326	4.7	0.001345	19 (19)
all Infants (<1 year old)		0.000133	5.1	0.000631	24	**0.002491**	**96 (94)**
children 1-2 years old		0.000138	5.3	0.000504	19	0.002043	79 (78)
children 3-5 years old		0.000112	4.3	0.000436	17	0.001761	68 (64)
children 6-12 years old		0.000078	1.1	0.000310	4.5	0.001281	19 (18)
youth 13-19 years old		0.000057	<1	0.000253	3.7	0.001060	15 (15)
adults 20-49 years old		0.000075	1.1	0.000328	4.8	0.001360	20 (19)
adults 50-99 years old		0.000071	1.0	0.000308	4.5	0.001227	18 (17)
females 13-49 years old		0.000074	1.1	0.000327	4.8	0.001340	19 (19)

[1] Risk estimates from the water only analysis are presented in parenthesis.

5.4.4 Chronic Dietary Risk Assessment

Since the peak AChEI occurs quickly and recovers within hours, repeated daily exposure does not result in increased inhibition of AChE as the enzyme recovery is complete before the next acute exposure. Therefore, only acute exposure durations are applicable for oxamyl and a chronic assessment is not required.

5.4.5 Cancer Dietary Risk Assessment

Oxamyl is classified as a "Group E" chemical based on lack of evidence of carcinogenicity in rats and mice; therefore, a cancer assessment is not required.

5.4.6 Commodity-Specific Analysis

While DEEM provides risk estimates for a population reflecting a range of serving sizes and range of residue levels, HED also conducted a CSA for oxamyl to determine whether there are

potentially significant dietary risk concerns resulting from single-serving size portions of specific foods. For example, there may be concern for commodities that are infrequently consumed or pesticides that may be used less frequently (e.g. low percent crop treated). CSA analyses provide risk estimates for an individual consuming a reasonable serving size of individual commodities bearing residues at levels found in PDP monitoring. Only the CSA analyses for infants and children are presented as they had the highest exposure, on a relative basis, for the lifestages evaluated. Using the maximum value of oxamyl residues found in PDP the exposure estimates for most commodities were below 100% of the aPAD with some exceptions. One cucumber sample (of 378 total samples), one bell pepper (of 1671 samples), and one summer squash (of 1426 samples) bore residues that resulted in exposure estimates of 110% of the aPAD[11]. Only two PDP samples had residues that resulted in exposure estimates greater than 110% of the aPAD for children 1-2, which were both for summer squash: one sample at 120% of the aPAD and one at 190% aPAD. Note that these reflect residues in/on uncooked commodities; cooking studies conducted with other NMCs, such as aldicarb, have shown reduction of residues when cooked using normal consumer practices.

6.0 Residential (Non-Occupational) Exposure/Risk Characterization

There are no registered uses of oxamyl at residential sites. Oxamyl is a restricted use pesticide and products containing oxamyl are intended for occupational use only at this time. As a result, a residential exposure and risk assessment was not conducted.

7.0 Non-Occupational Spray Drift Exposure and Risk Estimates

Off-target movement of pesticides can occur via many types of pathways and it is governed by a variety of factors. Sprays that are released and do not deposit in the application area end up off-target and can lead to exposures to those it may directly contact. They can also deposit on surfaces where contact with residues can eventually lead to indirect exposures (*e.g.*, children playing on lawns where residues have deposited next to treated fields). The potential risk estimates from these residues can be calculated using drift modeling onto 50-feet wide lawns coupled with methods employed for residential risk assessments for turf products.

The approach to be used for quantitatively incorporating spray drift into risk assessment is based on a premise of compliant applications which, by definition, should not result in direct exposures to individuals because of existing label language and other regulatory requirements intended to prevent them.[12] Direct exposures would include inhalation of the spray plume or being sprayed directly. Rather, the exposures addressed here are thought to occur indirectly through contact with impacted areas, such as residential lawns, when compliant applications are conducted. Given this premise, exposures for children (1 to 2 years old) and adults who have contact with turf where residues are assumed to have deposited via spray drift thus resulting in an indirect exposure are the focus of this analysis analogous to how exposures to turf products are considered in risk assessment.

In order to evaluate the drift potential and associated risks, an approach based on drift modeling coupled with techniques used to evaluate residential uses of pesticides was utilized. Essentially, a

[11] Serving sizes for these commodities were assumed to be ¼ cup for infants and ½ cup for children 1-2. Note that USDA currently recommends a total of 1 cup of vegetables each day for children 2-3. (https://www.choosemyplate.gov/vegetables ; accessed 6/13/17)

[12] This approach is consistent with the requirements of the EPA's Worker Protection Standard.

residential turf assessment based on exposure to deposited residues has been completed to address drift from the agricultural applications of oxamyl. In the spray drift scenario, the deposited residue value was determined based on the amount of spray drift that may occur at varying distances from the edge of the treated field using the AgDrift® (v2.1.1) model and the *Residential Exposure Assessment Standard Operating Procedures Addenda 1: Consideration of Spray Drift Policy*. Once the deposited residue values were determined, the remainder of the spray drift assessment was based on the algorithms and input values specified in the recently revised (2012) *Standard Operating Procedures For Residential Risk Assessment (SOPs)*.

For oxamyl, chemical-specific TTR data are not available, therefore, the estimated TTR are based on a default assumption from the 2012 Residential SOPs that the transferable residue available for exposure is 1% of the total deposited residue, which is assumed to be equivalent to the maximum application rate.

A screening approach was developed based on the use of the AgDrift® model in situations where specific label guidance that defines application parameters is not available.[13] AgDrift® is appropriate for use only when applications are made by aircraft, airblast orchard sprayers, and groundboom sprayers. When AgDrift® was developed, a series of screening values (i.e., the Tier 1 option) were incorporated into the model and represent each equipment type and use under varied conditions. The screening options specifically recommended in this methodology were selected because they are plausible and represent a reasonable upper bound level of drift for common application methods in agriculture. These screening options are consistent with how spray drift is considered in a number of ecological risk assessments and in the process used to develop drinking water concentrations used for risk assessment. In all cases, each scenario is to be evaluated unless it is not plausible based on the anticipated use pattern (e.g., herbicides are not typically applied to tree canopies) or specific label prohibitions (e.g., aerial applications are not allowed). In many cases, risks are of concern when the screening level estimates for spray drift are used as the basis for the analysis. In order to account for this issue and to provide additional risk management options additional spray drift deposition fractions were also considered. These drift estimates represent plausible options for pesticide labels.

Combined Risk Estimates from Lawn Deposition Adjacent to Applications

The spray drift risk estimates are based on an estimated deposited residue concentration as a result of the screening level agricultural application scenarios. Oxamyl is registered on various agricultural crops, and most of the registered products are applied either via aerial, chemigation, groundboom, airblast or with handheld equipment. The maximum application rate for applications via aerial and groundboom equipment is 4 lb ai/A, while the maximum application rate for applications via airblast equipment is 2 lb ai/A. The recommended drift scenario screening level options are listed below:

- **Groundboom applications** are based on the AgDrift® option for high boom height and using very fine to fine spray type using the 90th percentile results.
- **Orchard airblast applications** are based on the AgDrift® option for Sparse (Young/Dormant) tree canopies.
- **Aerial applications** are based on the use of AgDrift® Tier 1 aerial option for a fine to medium spray type and a series of other parameters which will be described in more detail below (e.g., wind vector assumed to be 10 mph in a downwind direction for entire application/drift event).

[13] http://www.agdrift.com/

In addition to the screening level spray drift scenarios described above, additional results are provided which represent viable drift reduction approaches that represent potential risk management options. In particular, different spray qualities have been considered as well as the impact of other application conditions (e.g., boom height, use of a helicopter instead of fixed wing aircraft, crop canopy conditions).

Dermal risk estimates were calculated for adults (LOC = 10). Dermal and incidental oral risk estimates for children (1 to <2 years old) were combined because the toxicity endpoint for each route of exposure is the inhibition of RBC AChE. For children, the LOC for dermal and incidental oral exposures is 26.

Adult dermal and children's (1 to < 2 year old) dermal and incidental oral risk estimates related to spray drift result in a range of distances from the edge of the field necessary to reach the target MOE, depending on the spray drift scenario. These are summarized in Table 7.1 (all drift calculations are provided in Appendix D of the occupational and residential exposure (ORE) memo as excel files). Results indicate that aerial applications provided the highest risk estimates from spray drift. Appropriate drift reduction techniques, such as changing the spray type/nozzle configuration to coarser spray applications may result in less drift and reduced risk concerns (i.e., higher MOEs) from aerial applications. Similarly, using coarser sprays and lowering boom height for groundboom sprayers reduces risk concerns.

Table 7.1. Summary of Spray Drift Buffers for Oxamyl.

Scenario	Crop Category	Application rate (lb ai/A)	Adult Buffer Summary	Children 1 < 2 years Buffer Summary (Dermal + Incidental Oral)
			Distance from Edge of Field Necessary to Reach MOE of 10	Distances from Edge of Field Necessary to Reach combined MOEs >26
Aerial	Typical Field Crops	4	0 to 50	125 to >300
	Typical and High Acreage Crops	2	0	50 to >300
	Typical Field Crops, High Acreage Field Crops, and Orchard Crops	1	0	25 to >300
	Typical and High Acreage Crops	0.5	0	10 to >150
Groundboom	Typical Field Crops	4	0	10 to >100
	Typical and High Acreage Crops	2	0	0 to >50
	Typical and High Acreage Crops	1	0	0 to >25
	Typical and High Acreage Crops	0.5	0	0 to >10
Airblast	Orchard Crops	2	0	0 to >50
		1	0	0 to >25

8.0 Non-Occupational Bystander Post-Application Inhalation Exposure and Risk Estimates

Volatilization of pesticides may be a source of post-application inhalation exposure to individuals nearby pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its FIFRA Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010[14]. The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis[15]. During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies) or further analysis are required for oxamyl.

[14] http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html
[15] http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219

9.0 Aggregate Exposure/Risk Characterization

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure. The registered uses of oxamyl are not anticipated to result in residential exposure and thus the dietary (food and drinking water) exposure and risk estimates provided in Section 5.4.3 represent the aggregate exposure and risk estimates.

10.0 Cumulative Exposure/Risk Characterization

The FQPA requires the Agency to consider the cumulative risks of chemicals sharing a common mechanism of toxicity. Oxamyl is a member of the NMC common-mechanism group. NMCs like oxamyl share the ability to inhibit AChE through carbamylation of the serine residue on the enzyme leading to accumulation of acetylcholine and ultimately cholinergic neurotoxicity. This shared MOA/AOP is the basis for the NMC common mechanism grouping per OPP's *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999). The 2007 CRA and the subsequent revision used brain AChEI in female rats as the source of dose response data for the relative potency factors and PODs for each NMC, including oxamyl. Prior to the completion of Registration Review, OPP will update the NMC CRA to incorporate new toxicity and exposure information available since 2007.

The most recent cumulative risk assessment for the NMC carbamates was issued for comment on September 26, 2007 and is available on the Agency website[16].

Prior to a final registration review decision for oxamyl, the Agency will determine if there is any new information, such as new hazard or exposure data or information on changes to the use pattern, which would affect the cumulative risk assessment. Should the Agency determine that new information on oxamyl is available that could potentially impact the cumulative risk assessment and result in a risk of concern, the Agency will revisit the cumulative risk assessment.

11.0 Occupational Exposure/Risk Characterization

Oxamyl is registered for use on a variety of agricultural commodities. There are two registered oxamyl end-use product labels: DuPont™ Vydate® L (EPA Reg. #352-372) and DuPont™ Vydate® C-LV (EPA Reg. #352-532). Both products are liquid formulations and are RUPs that may be applied via groundboom sprayer, aerial equipment, airblast sprayer, chemigation, and handheld sprayers. Application rates for oxamyl range from 0.5 to 4 lb ai/acre. Oxamyl can be applied from one to eight times a year, depending on the crop. Maximum seasonal application rates range from 2 to 10 lb ai/A. A summary of occupational uses (agricultural and non-agricultural) is listed in Appendix F. Based on the registered application scenarios and toxicological considerations, non-cancer occupational handler (dermal and inhalation) and occupational post-application (dermal) assessments were conducted. The registered uses of oxamyl resulting in occupational exposure were evaluated by HED and reviewed by the HED

[16] http://itrcweb.org/FileCabinet/GetFile?fileID=6883

Exposure Science Advisory Committee (ExpoSAC) (L. Venkateshwara, 20-JUN-2017; D440797).

11.1 Occupational Handler Exposure/Risk Estimates

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

The quantitative exposure/risk assessment developed for occupational handlers is based on the following scenarios which represent all the registered uses of oxamyl:

- Mixing/loading liquids to support aerial, groundboom, chemigation, and airblast applications;
- Applying sprays with aircraft, groundboom, and airblast equipment;
- Flagging to support aerial spray applications; and
- Mixing/loading/applying liquids via backpack sprayer.

Exposure Duration: HED typically classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. Exposure duration is determined by many things, including the exposed population, the use site, the pest pressure triggering the use of the pesticide, and the cultural practices surrounding that use site. For most agricultural uses, it is reasonable to believe that occupational handlers will not apply the same chemical every day for more than a one-month time frame; however, there may be a large agribusiness and/or commercial applicators who may apply a product over a period of weeks (e.g., completing multiple applications for multiple clients within a region). For oxamyl, based on the registered uses, short- and intermediate-term exposures are expected since multiple applications (up to eight per season) can be made on various crops. As mentioned previously, only acute exposures or a series of acute exposures are of concern for oxamyl; therefore, the same endpoint has been selected for all durations of an exposure route. As a result, short-term assessments are considered protective of intermediate-term assessments.

Mitigation/Personal Protective Equipment: Estimates of dermal and inhalation exposure were calculated for various levels of PPE. Results are presented for "baseline," defined as a single layer of clothing consisting of a long sleeved shirt, long pants, shoes plus socks, no protective gloves, and no respirator, as well as baseline with various levels of PPE as necessary (e.g., gloves, respirator, etc.). The oxamyl registered labels require handlers to wear coveralls over a single layer of clothing (long sleeved shirt and long pants), chemical-resistant gloves, chemical-resistant footwear, protective eyewear, chemical-resistant headgear for overhead exposure, chemical-resistant apron when cleaning equipment, mixing, or loading, and a respirator with an organic vapor-removing cartridge with a pre-filter approved for pesticides, a canister approved for pesticides, or a National Institute for Occupational Safety and Health (NIOSH) approved respirator with an organic vapor (OV) cartridge or canister with any R (resistant to oils), P (oil proof) or HE (high efficiency) pre-filter. In addition, the DuPont™ Vydate® C-LV label requires mixers and loaders supporting aerial use on cotton in California and Arizona to use a closed system according to the requirements listed in the Worker Protection Standards (WPS) for Agricultural Pesticide (40 CFR 170.24(d)(4)).

Occupational Handler Non-Cancer Exposure and Risk Estimate Equations

The algorithms used to estimate non-cancer exposure and dose for occupational handlers can be found in Appendix A of the ORE memo (L. Venkateshwara, 20-JUN-2017; D440797).

Combining Exposures/Risk Estimates

Since the toxicological effects are the same (RBC cholinesterase inhibition) for the dermal and inhalation PODs, the dermal and inhalation risks to handlers are combined. Since the LOC is 10 for dermal risks and 30 for inhalation risks, an ARI is calculated. The LOC for an ARI is 1 (i.e., ARIs greater than 1 are not a concern). ARIs are calculated using the following formula:

Aggregated Risk Index (ARI) = 1 / [(LOC/Dermal MOE) + (LOC /Inhalation MOE)).

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates

The occupational handler exposure and risk estimates indicate that the dermal and inhalation risk estimates are not of concern (i.e., ARIs ≥ 1) for most scenarios assuming the use of label-required PPE (noted by the highlighted column in Table 11.1.1 – double layer of clothing, gloves, a chemical-resistant hat for airblast applications, and a PF10 respirator). Seven scenarios (out of 53) do not reach an acceptable ARI with label PPE.

To further characterize the risks of concern, the inhalation and dermal MOEs for scenarios that result in risks of concern with label-specified PPE (double layer of clothing, gloves, a chemical-resistant hat for airblast applications, and a PF10 respirator) are summarized Table 11.1.2. Two scenarios do not reach an acceptable ARI despite consideration of the highest level of mitigation available (i.e., engineering controls). These scenarios are mixing/loading liquids for aerial applications for high acreage crops (at 2.0 lb ai/A) and mixing, loading and applying liquids with backpack sprayer to orchard crops (bananas and plantains). The second scenario has an ARI <1 at label-specified PPE (double layer of clothing, gloves and PF10 respirator), which is the maximum PPE available for this type of application. Note, in this assessment all rates were assessed and lower rates resulted in lower risk estimates of concern and less PPE to be not of concern.

HED has no data to assess exposures to pilots using open cockpits. The only data available are for exposure to pilots in enclosed cockpits. Therefore, risks to pilots are assessed using the engineering control (enclosed cockpits) and baseline attire (long-sleeve shirt, long pants, shoes, and socks); per the Agency's WPS stipulations for engineering controls, pilots are not required to wear protective gloves for the duration of the application. With this level of protection, there are no risk estimates of concern for applicators.

The Agency matches quantitative occupational exposure assessment with appropriate characterization of exposure potential. While HED presents quantitative risk estimates for human flaggers where appropriate, agricultural aviation has changed dramatically over the past two decades. According the 2012 National Agricultural Aviation Association (NAAA) survey of their membership, the use of Global Positioning System (GPS) for swath guidance in agricultural aviation has grown steadily from the mid 1990s. Over the same time period, the use of human flaggers for aerial pesticide applications has decreased steadily from ~15% in the late 1990s to only 1% in the most recent (2012) NAAA survey. The Agency will continue to monitor all

available information sources to best assess and characterize the exposure potential for human flaggers in agricultural aerial applications.

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Oxamyl.

Exposure Scenario	Crop or Target[1,2,3]	Dermal Unit Exposure (µg/lb ai)[4]	Inhalation Unit Exposure (µg/lb ai)[4]	Maximum Application Rate[5]	Area Treated[6]	ARI[7] SL/No G No-R	SL/G No-R	DL/G No-R	SL/No G PF5 R	SL/G PF5-R	DL/G PF5-R	SL/No G PF10 R	SL/G PF10-R	DL/G PF10-R	EC
Mixer/Loader															
Liquids for aerial application	Orchard	SL/No G 220 SL/G 37.6 DL/G 29.1 EC 8.6	No-R 0.219 PF5 R 0.0438 PF10 R 0.0219 EC 0.083	1	350	**0.34**	1.6	2	**0.36**	2	2.5	**0.36**	2	2.6	6.2
	Field crop, typical			4		**0.086**	**0.41**	**0.5**	**0.089**	**0.49**	**0.63**	**0.09**	**0.51**	**0.66**	1.6
				2		**0.17**	**0.79**	1	**0.18**	**0.95**	1.3	**0.18**	0.97	1.3	3.1
				1		**0.34**	1.6	2	**0.36**	2	2.5	**0.36**	2	2.6	6.2
				0.5		**0.69**	**3.3**	3.9	**0.71**	4	5	0.72	4.1	5.2	12
	Field crop, high-acreage			2	1200	**0.05**	**0.24**	**0.29**	**0.051**	**0.29**	**0.36**	**0.052**	**0.3**	**0.38**	**0.89**
				1		**0.096**	**0.47**	**0.58**	**0.099**	**0.58**	**0.74**	**0.1**	**0.59**	**0.76**	1.8
				0.5		**0.2**	**0.94**	1.2	**0.21**	1.1	1.5	**0.21**	1.2	1.5	3.6
Liquids for airblast application	Orchard			2	40	1.5	7.2	8.8	1.6	8.7	11	1.6	8.9	12	27
				1		3	14	17	3.1	17	22	3.1	18	23	54
Liquids for chemigation	Orchard			2	350	**0.17**	**0.79**	1	**0.18**	**0.95**	1.3	**0.18**	**0.97**	1.3	3.1
				1.34		**0.26**	1.2	1.5	0.27	e1.5	1.9	**0.27**	1.6	1.9	4.6
				0.5		**0.34**	1.6	2	0.36	2	2.5	**0.36**	2	2.6	6.2
	Field crop, typical			4		**0.086**	**0.41**	**0.5**	**0.089**	**0.49**	**0.63**	**0.09**	**0.51**	**0.66**	1.6
				2		**0.17**	**0.79**	1	**0.18**	**0.95**	1.3	0.18	0.97	1.3	3.1
				1		**0.34**	1.6	2	**0.36**	2	2.5	**0.36**	2	2.6	6.2
				0.5		**0.69**	3.3	3.9	**0.71**	4	5	**0.72**	4.1	5.2	12
	Field crop, high-acreage			2		**0.17**	**0.79**	1	**0.18**	**0.95**	1.3	**0.18**	**0.97**	1.3	3.1
				1		**0.34**	1.6	2	**0.36**	2	2.5	**0.36**	2	2.6	6.2
				0.5		**0.69**	3.3	3.9	**0.71**	4	5	**0.72**	4.1	5.2	12
Liquids for Groundboom	Field crop, typical			4	80	**0.37**	1.8	2.2	**0.39**	2.2	2.8	**0.39**	2.2	2.9	6.8
				2		**0.74**	3.6	4.3	**0.77**	4.3	5.5	**0.78**	4.5	5.7	14
				1		1.5	7.2	8.8	1.6	8.7	11	1.6	8.9	12	27
				0.5		3	14	17	3.1	17	22	3.1	18	23	54
	Field crop, high-acreage			2	200	**0.3**	1.4	1.7	**0.31**	1.7	2.2	**0.31**	1.8	2.3	5.4
				1		**0.6**	2.9	3.5	**0.62**	3.5	4.4	**0.63**	3.6	4.5	11
				0.5		1.2	5.7	6.9	1.3	6.9	8.9	1.3	7.1	9.2	22
Applicator															
Aerial applications	Orchard	EC 2.08	EC 0.0049	1	350	No data									200
	Field crop, typical			4											8.5
				2											17
				1											34
				0.5											68
	Field crop, high-acreage			2	1200										4.9
				1											9.9
				0.5											20
Airblast applications	Orchard	SL/No G 1,770 SL/G 1,590 (SL/G/CRH 215) DL/G 1,480 (DL/G/CRH 141) EC 14.6	No-R 4.71 PF5 R 0.942 PF10 R 0.471 EC 0.068	2	40	**0.17**	**0.19**	**0.2**	**0.19**	**0.21**	**0.22**	**0.19**	**0.22**	**0.23**	19
				1		**0.35**	**0.38**	**0.41**	**0.38**	**0.42**	**0.46**	**0.38**	**0.42**	**0.46**	38

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Oxamyl.

Exposure Scenario	Crop or Target[1,2,3]	Dermal Unit Exposure (µg/lb ai)[4]	Inhalation Unit Exposure (µg/lb ai)[4]	Maximum Application Rate[5]	Area Treated[6]	ARI[7]									
						SL/No G No-R	SL/G No-R	DL/G No-R	SL/No G PF5 R	SL/G PF5-R	DL/G PF5-R	SL/No G PF10 R	SL/G PF10-R	DL/G PF10-R	EC
Groundboom applications	Field crop, typical	SL/No G 78.6 SL/G 16.1 DL/G 12.6 EC 5.1	No-R 0.34 PF5 R 0.068 PF10 R 0.034 EC 0.043	4	80	15	42	47	17	71	86	18	78	97	190
				2		3.6	10	12	4.2	17	21	4.3	19	24	48
				1		7.2	21	23	8.4	36	43	8.6	39	48	98
				0.5		9.9	28	32	12	47	58	12	52	65	130
	Field crop, high-acreage			2	200	2.4	7	7.9	2.8	12	14	2.8	13	16	32
				1		3.6	10	12	4.2	17	21	4.3	19	24	48
				0.5		15	42	47	17	71	86	18	78	97	190
Flagger															
Flagging for aerial applications	Orchard	SL/No G 11 SL/G 12 DL/G 10.6	No-R 0.35 PF5 R 0.07 PF10 R 0.035	1	350	16	16	17	32	30	33	36	33	37	NA
	Field crop, typical			4		**0.71**	**0.67**	**0.72**	1.4	1.2	1.4	1.6	1.4	1.6	NA
				2		1.4	1.4	1.4	2.8	2.6	2.8	3.1	2.9	3.2	NA
				1		2.8	2.7	2.9	5.5	5.1	5.6	6.2	5.8	6.4	NA
				0.5		5.6	5.4	5.8	11	10	11	12	11	13	NA
	Field crop, high-acreage			2		1.4	1.4	1.4	2.8	2.6	2.8	3.1	2.9	3.2	NA
				1		2.8	2.7	2.9	5.5	5.1	5.6	6.2	5.8	6.4	NA
				0.5		5.6	5.4	5.8	11	10	11	12	11	13	NA
Mixer/Loader/Applicator															
M/L/A liquids ground applications (soil directed) with backpack	Orchard (bananas and plantains only)	SL/No G 8,260 SL/G 8,260 DL/G 4,120	No-R 2.58 PF5 R 0.516 PF10 R 0.258	3.6[8]	2[9]	**0.45**	**0.45**	**0.9**	**0.46**	**0.46**	**0.92**	**0.46**	**0.46**	**0.93**	NA

Shaded column = current PPE required on labels. Bold values indicate the LOC has been exceeded.

1. Orchard: Apple, Citrus, Nonbearing Fruit (apple, cherry, citrus, peach, pear).
2. Typical field crops: @ 4 lb ai/A: Cucumber, Cantaloupe, Honeydew Melon, Watermelon, Squash, Pumpkin, Onions (dry bulb only); @2 lb ai/A: Cucumber, Cantaloupe, Honeydew Melon, Watermelon, Squash, Pumpkin, Tomatoes; @1 lb ai/A: Celery, Cucumber, Cantaloupe, Honeydew Melon, Watermelon, Squash, Pumpkin, Garlic, Onions (dry bulb only), Peppers, Tomatoes; @ 0.5 lb ai/A: Onions (dry bulb only), Peppers.
3. High-acreage field crops: @2 lb ai/A: Peppermint and Spearmint, Potatoes; @1 lb ai/A: Clover grown for seed, Cotton, Peppermint and Spearmint, Potatoes; @ 0.5 lb ai/A: Cotton, Peanuts.
4. Based on the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (November 2016); Level of mitigation: SL/No G No-R = Single layer clothing, no gloves, no respirator; SL/G No-R = Single layer clothing, gloves, no respirator; DL/G No-R = Double layer clothing, gloves, no respirator; SL/No G PF5 R = Single layer clothing, no gloves, PF5 respirator; SL/G PF5 R = Single layer clothing, gloves, PF5 respirator; DL/G PF5 R = Double layer clothing, gloves, PF5 respirator; SL/No G PF10 R = Single layer clothing, no gloves, PF10 respirator; SL/G PF10 R = Single layer clothing, gloves, PF10 respirator; DL/G PF10 R = Double layer clothing, gloves, PF10 respirator; EC = Engineering Controls. ND = no data.
5. Based on registered labels.
6. ExpoSAC Policy #9.1.
7. ARI = 1 ÷ (Dermal LOC/Dermal MOE) + (Inhalation LOC/Inhalation MOE). Dermal LOC = 10. Inhalation LOC = 30.
8. According to information provided by DuPont, there are approximately 715 banana plants per acre and a person can apply oxamyl with a spotgun to approximately 2 acres per day. Since 10 mL of concentrate is applied per plant, then 3.6 pounds active ingredient is applied per acre.
9. According to information provided by DuPont, there are approximately 715 banana plants per acre and a person can apply oxamyl with a spotgun to approximately 2 acres per day. Since 10 mL of concentrate is applied per plant, then 3.6 pounds active ingredient is applied per acre

11.1.2. Summary of Scenarios that are of Concern with Label-Specified PPE[1].									
Exposure Scenario	**Crop or Target**	**Maximum Application Rate**	**Area Treated**	**MOE Dermal Label PPE**	**MOE Inhalation Label PPE**	**ARI Label PPE**	**MOE Dermal Engineering Control**	**MOE Inhalation Engineering Control**	**ARI Engineering Control**
Mixing/loading liquids for aerial application	Field crop, typical	4	350 acres	**6.8**	550	**0.66**	23	150	1.6
	Field Crop, high acreage	2	1200 acres	**3.9**	320	**0.38**	13	85	**0.89**
		1		**7.9**	640	**0.76**	27	170	1.8
Mixing/loading liquids for chemigation	Field crop typical	4	350 acres	**6.8**	550	**0.66**	23	150	1.6
Airblast applications[1]	Orchard	2	40 acres	**2.3**	450	**0.23**	240	3,100	19
		1		**4.7**	900	**0.46**	470	6,200	38
M/L/A liquids ground applications (soil directed) with backpack	Orchard	3.6	2	**9.3**	9,100	**0.93**	No data	No data	NA

Bold values indicate the LOC has been exceeded (Dermal MOEs < 10; Inhalation MOEs < 30. ARI < 1).

[1] Double layer of clothing, gloves, a chemical-resistant hat for airblast applications, and a PF10 respirator

11.2 Occupational Post-Application Exposure/Risk Estimates

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for post-application exposure.

11.2.1 Occupational Post-Application Inhalation Exposure/Risk Estimates

There are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from its FIFRA SAP in December 2009, and received the SAP's final report on March 2, 2010[17]. The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis[18]. During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies) or further analysis is required for oxamyl.

In addition, the Agency is continuing to evaluate the available post-application inhalation exposure data generated by the ARTF. Given these two efforts, the Agency will continue to identify the need for and, subsequently, the way to incorporate occupational post-application inhalation exposure into the Agency's risk assessments.

11.2.2 Occupational Post-Application Dermal Exposure/Risk Estimates

Occupational Post-Application Dermal Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the occupational post-application risk assessments. Each assumption and factor is detailed below.

Exposure Duration: HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. For oxamyl, based on the registered uses, short- and intermediate-term exposures are expected since the product can be applied multiple times over the course of a growing season. The toxicological database for oxamyl indicates that the magnitude of AChEI does not increase with repeated exposures; therefore, the same endpoint was selected to evaluate short- and intermediate-term. As a result, the short-term assessment is considered protective of the intermediate-term exposures.

[17] http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html.
[18] http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219.

Transfer Coefficients: It is the policy of HED to use the best available data to assess post-application exposure. Sources of generic post-application data, used as surrogate data in the absence of chemical-specific data, are derived from ARTF exposure monitoring studies, and, as proprietary data, are subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting post-application exposure that are used in this assessment, known as "transfer coefficients," are presented in the ExpoSAC Policy 3[19]" which, along with additional information about the ARTF data, can be found at the Agency website[20]. For use on cotton, HED has also assessed the post-application dermal exposure and risk estimates for workers involved in harvesting cotton bolls. Although most of cotton harvesting is done mechanically, there are still some activities with the potential for exposure, that are associated with the harvesting of cotton. These recommended transfer coefficients are also presented in the ExpoSAC Policy 3.

Application Rate: The application rates used in this assessment are provided in Appendix F.

Exposure Time: The average occupational workday is assumed to be 8 hours.

DFR Data: Chemical-specific DFR data have been submitted for oxamyl. Three studies (see below) were submitted that examined residues of oxamyl on the following crops: tomatoes, citrus, and cucumber. All three studies have been reviewed by HED (see Appendix B of the ORE memo and D378340) and found to be acceptable for risk assessment. The three DFR studies are as follows:

- "Dissipation of Dislodgeable Foliar and Soil Residues of Oxamyl Following Application of Vydate® L Insecticide to Tomatoes in the USA- Season 1997 and 1998;" MRID 44704801.
- "Dissipation of Dislodgeable Foliar Residues of Oxamyl from Citrus Following Application of Vydate® L Insecticide in the U.S.A - Season 1997;" MRID 44686901.
- "Dissipation of Dislodgeable Foliar Residues of Oxamyl from Cucumbers Following Application of Vydate® L Insecticide in the U.S.A. - Season 1997;" MRID 44686902.

Use of the DFR data:

Table 11.2.2.1 provides a summary of how the available DFR data were used in the post-application assessment.

- The citrus DFR study data was used to assess exposure to oxamyl-treated foliage for citrus, as well as other tree crops (pears, apples, bananas, plantains, and non-bearing trees).
- The cucumber DFR study data was used to assess exposure to oxamyl-treated foliage for the cucurbit crops.
- The tomato DFR study data were used to assess exposure to oxamyl-treated foliage for tomatoes and other fruiting vegetables (peppers and eggplant).
- For all the remaining crops, both the tomato residue data *and* the cucumber residue data were used to assess exposure to oxamyl-treated foliage. For all crops where both tomato

[19] Available: http://www.epa.gov/pesticides/science/exposac_policy3.pdf
[20] Available: http://www.epa.gov/pesticides/science/post-app-exposure-data.html

and cucumber residue data are presented, the results for the California sites were averaged and the results from the Florida and Georgia sites were averaged.

Table 11.2.2.1. Summary of DFR Data Use in Occupational Post-Application Assessment for Oxamyl.

Crop for which DFR data available	Locations included in study	Crops for which DFR data used as surrogate
Tomatoes	CA and FL	Tomatoes, Peppers (Bell and Non-Bell), Eggplant Celery, Cotton, Peanuts, Peppermint/Spearmint, Potatoes, Sweet potatoes, Yam, Tobacco, Clover grown for seed, Garlic, Ginger Root, Onions, Pineapple
Citrus	CA and FL	Apples, Bananas/Plantains, Citrus, Nonbearing Fruit (apple, cherry, citrus, peach, pear), Pears
Cucumber	CA and GA	Cucumber, Cantaloupe, Honeydew Melon, Watermelon, Squash, Pumpkin Celery, Cotton, Peanuts, Peppermint/Spearmint, Potatoes, Sweet potatoes, Yam, Tobacco, Clover grown for seed, Garlic, Ginger Root, Onions, Pineapple
Tomato and Cucumber	FL and GA (average)	Tomato, Eggplant, Pepper Chilli and Bell), Sweet Potato, Celery, Mint (Spearmint and Peppermint), Pineapple, Potato, Tobacco, Cotton, Forage Crop, Bulb Onion, Peanut

Use of dislodgeable boll residue (DBR) data for cotton harvesting

- There are no chemical-specific data available for the amount of residue available on the cotton bolls (i.e., DBR); however, surrogate data are available from a study with the active ingredient tribufos (MRID 42701601). The residue data from this study were reviewed previously and found to be appropriate for use in risk assessment (B. Tarplee, 3/12/1997, D227007). The average DBR levels (µg/50-gram sample) were analyzed using linear regression to estimate the dissipation over time. Since the oxamyl labels include a 28-day pre-harvest interval, the 28-day predicted cotton boll residue data for that timeframe was presented as surrogate data for this assessment and then adjusted for the difference in application rates between the study and label.

Occupational Post-Application Non-Cancer Dermal Exposure and Risk Estimate Equations

The algorithms used to estimate non-cancer exposure and dose for occupational post-application workers can be found in Appendix A of the ORE memo (L. Venkateshwara, 20-JUN-2017; D440797).

Occupational Post-Application Non-Cancer Dermal Risk Estimates

The post-application exposure scenarios associated with the registered uses of oxamyl are summarized in Tables 11.2.2.2 through 11.2.2.6. The results of the risk assessment for post-application exposures indicate that the location and/or the environmental conditions (i.e., arid versus non-arid) near the time of application influence the length of time following application until risks are below HED's LOC (i.e., MOEs are greater than or equal to 10) as does the type of plant to which the application is directed. For most crops, the post-application assessment indicates that following applications in arid areas (i.e., outdoor areas where average annual rainfall is less than 25 inches), residues persist longer than in non-arid areas. Based on the current exposure assessment, post-application MOEs range from 1.3 to 500 on the day of

application, and do not reach acceptable MOEs until anywhere from 12 hours after application up to 7 days after application (most of the exceedances of the current REI is for handset irrigation).

- For the tree crops, using the citrus DFR data, MOEs range from 2.4 to 170 on the day of application. Some crop/activity combinations do not reach an acceptable MOE (LOC = 10) until 7 days after application.
- For the cucurbit crops, using the cucumber DFR data, MOEs range from 2.4 to 100 on the day of application. Some crop/activity combinations do not reach an acceptable MOE (LOC = 10) until 5 days after application.
- For tomatoes and other fruiting vegetable crops, using the tomato DFR data, MOEs range from 2.6 to 280 on the day of application. Some crop/activity combinations do not reach an acceptable MOE (LOC = 10) until 2 days after application.
- For other vegetable and non-tree fruit crops, using the tomato and cucumber DFR data MOEs range from 1.2 to 500 on the day of application. Some crop/activity combinations do not reach an acceptable MOE (LOC = 10) until 4 days after application.
- For activities associated with cotton harvesting, using DBR data, MOEs were not of concern on the day of application (i.e., MOEs ≥ 10) except the tramper activities with a MOE of 8.9 (Table 11.2.2.6). The tramper activities reached an acceptable MOE after a 1-day REI, as presented in Table 11.2.2.6. Assuming the current pre-harvest interval (PHI) of 14 days for cotton, there are no risks of concern for activities associated with cotton harvesting.

Table 11.2.2.2. Oxamyl Post-Application Risks for Tree Crops using Citrus DFR Data (MRID 44686901).

Crop	Application rate (lb ai/A)	Activity	TC (cm^2/hr)	DFR on Day 0[a] (ug/cm^2)	MOE on Day 0[b]	Day at which MOE ≥10
				CA	CA	CA
Apple, Cherry, Peach, Pear	2	Weeding, Hand Propping Orchard maintenance Weeding, Hand	100	4.06	85	0 (12 hours)
		Transplanting	230		37	
		Scouting Pruning, Hand Training Pruning, Hand	580		15	
		Harvesting, Hand	1400		**6.1**	1
		Thinning Fruit	3600		**2.4**	7
Apple, Cherry, Grapefruit, Lemon, Orange, Peach, Pear	1	Weeding, Hand Propping Orchard maintenance Weeding, Hand	100	2.03	170	0 (12 hours)
		Transplanting	230		74	0 (12 hours)
		Scouting Pruning, Hand Training Pruning, Hand	580		29	0 (12 hours)
		Harvesting, Hand	1400		12	0 (12 hours)
		Thinning Fruit	3600		**4.7**	1
Banana/Plantain	1.34	Weeding, Hand	100	2.72	130	0 (12 hours)
		Harvesting, Hand	1400		**9.1**	1

Bold MOE values are below the LOC of 10.

a. DFR = residue values from citrus DFR study; adjusted to account for application rate differences.

b. MOE = POD (0.069 mg/kg/day) / Daily Dermal Dose. DAF is 2%.

Table 11.2.2.3. Oxamyl Post-Application Risks for Cucurbit Crops using Cucumber DFR Data (MRID 44686902).

Crop	Application rate (lb ai/A)	Activity	TC (cm^2/hr)	DFR on Day 0[a] (ug/cm^2)	MOE on Day 0[b]	Day at which MOE ≥10
				CA	CA	CA
Cantaloupe Cucumber Pumpkin Squash, summer Squash, winter Watermelon	1	Scouting Weeding, Hand Pruning, Hand Thinning Fruit	90	3.75	100	0 (12 hours)
		Transplanting	230		40	0 (12 hours)
		Harvesting, Hand Harvesting, Mechanically-assisted Turning Training	550		19	0 (12 hours)
		Irrigation (hand set)	1900		**4.8**	3
Cantaloupe Cucumber Pumpkin Squash, summer Squash, winter Watermelon	2	Scouting Weeding, Hand Pruning, Hand Thinning Fruit	90	7.5	51	0 (12 hours)
		Transplanting	230		20	0 (12 hours)
		Harvesting, Hand Harvesting, Mechanically-assisted Turning Training	550		**8.4**	2
		Irrigation (hand set)	1900		**2.4**	5

Bold MOE values are below the LOC of 10.

a. DFR = residue values from cucumber DFR study; adjusted to account for application rate differences.

b. MOE = POD (0.069 mg/kg/day) / Daily Dermal Dose. DAF is 2%.

Table 11.2.2.4. Oxamyl Post-Application Risks Fruiting Vegetables Crops using Tomato DFR Data (MRID 44704801).

Crop	Application rate (lb ai/A)	Activity	TC (cm^2/hr)	DFR on Day 0[a] (ug/cm^2)	MOE at Day 0[b]	Day at which MOE ≥10
				CA	CA	CA
Tomato	2	Pruning, Hand Weeding, Hand	70	7.04	70	0 (12 hours)
		Scouting	210		23	0 (12 hours)
		Transplanting	230		21	0 (12 hours)
		Harvesting, Hand Tying/Training	1100		**4.5**	1
		Irrigation (hand set)	1900		**2.6**	2
Eggplant	1	Pruning, Hand Scouting Weeding, Hand Thinning Fruit	90	3.52	110	0 (12 hours)
		Transplanting	230		43	0 (12 hours)
		Harvesting, Hand Tying/Training	550		18	0 (12 hours)
		Irrigation (hand set)	1900		**5.2**	1
Tomato Pepper, chili Pepper, bell	1	Pruning, Hand Weeding, Hand	70	3.52	140	0 (12 hours)
		Scouting	210		47	0 (12 hours)

Table 11.2.2.4. Oxamyl Post-Application Risks Fruiting Vegetables Crops using Tomato DFR Data (MRID 44704801).

Crop	Application rate (lb ai/A)	Activity	TC (cm^2/hr)	DFR on Day 0[a] (ug/cm^2)	MOE at Day 0[b]	Day at which MOE ≥10
				CA	CA	CA
		Transplanting	230		43	0 (12 hours)
		Harvesting, Hand Tying/Training	1100		**8.9**	1
		Irrigation (hand set)	1900		**5.2**	1
Pepper, chili Pepper, bell	0.5	Weeding, Hand	70	1.76	280	0 (12 hours)
		Scouting	210		93	0 (12 hours)
		Transplanting	230		85	0 (12 hours)
		Harvesting, Hand Tying/Training	1100		18	0 (12 hours)
		Irrigation (hand set)	1900		18	0 (12 hours)

Bold MOE values are below the LOC of 10.

a. DFR = residue values from tomato DFR study; adjusted to account for application rate differences.

b. MOE = POD (0.069 mg/kg/day) / Daily Dermal Dose. DAF is 2%.

Table 11.2.2.5. Oxamyl Post-Application Risks for Vegetable and Non-Tree Fruit Crops using Tomato and Cucumber DFR Data (MRID 44686902 and 44704801).

Crop	Application rate (lb ai/A)	Activity	TC (cm^2/hr)	DFR on Day 0[a] (ug/cm^2)		MOE at Day 0[b]		Day at which MOE ≥10
				Tomato FL	Cucumber GA	Tomato FL	Cucumber GA	Average of FL and GA residues
Potato, Sweet	4	Weeding, Hand	70	3.52	14.2	140	35	0 (12 hours)
		Scouting	210			47	12	0 (12 hours)
		Transplanting	230			43	11	0 (12 hours)
		Irrigation (hand set)	1900			**5.2**	**1.3**	5
Celery (FL and Rio Grande Valley of TX)	2	Weeding, Hand	70	3.96	7.1	120	69	0 (12 hours)
		Scouting	210			41	23	0 (12 hours)
		Transplanting	230			38	21	0 (12 hours)
		Harvesting, Hand	1100			**7.9**	**4.4**	3
		Irrigation (hand set)	1900			**4.6**	**2.6**	4
Mint (spearmint and peppermint)	2	Weeding, Hand	70	3.96	7.1	120	69	0 (12 hours)
		Scouting	1100			**7.9**	**4.4**	2
		Irrigation (hand set)	1900			**4.6**	**2.6**	4
Pineapple	2	Weeding, Hand	70	3.96	7.1	120	69	0 (12 hours)
		Scouting	210			41	23	0 (12 hours)
		Harvesting, Hand	1100			**7.9**	**4.4**	3
Potato (MD, NY, PA)	2	Weeding, Hand	70	3.96	7.1	120	69	0 (12 hours)
		Scouting	210			41	23	0 (12 hours)
		Irrigation (hand set)	1900			**4.6**	**2.6**	4
Tobacco	2	Weeding, Hand Scouting	90	3.96	7.1	97	54	0 (12 hours)
		Transplanting	230			38	**21**	0 (12 hours)
		Harvesting, Hand Harvesting, Mechanically-assisted Canopy Management	800			11	**6.1**	2
		Irrigation (hand set)	1900			**4.6**	**2.6**	4
Celery (MI, OH, PA, TX (except the Rio	1	Weeding, Hand	70	1.98	3.55	250	140	0 (12 hours)
		Scouting	210			83	46	0 (12 hours)
		Transplanting	230			76	42	0 (12 hours)
		Harvesting, Hand	1100			16	**8.8**	2

Table 11.2.2.5. Oxamyl Post-Application Risks for Vegetable and Non-Tree Fruit Crops using Tomato and Cucumber DFR Data (MRID 44686902 and 44704801).

Crop	Application rate (lb ai/A)	Activity	TC (cm^2/hr)	DFR on Day 0[a] (ug/cm^2)		MOE at Day 0[b]		Day at which MOE ≥10
				Tomato FL	Cucumber GA	Tomato FL	Cucumber GA	Average of FL and GA residues
Grande Valley, AZ, CA, FL)		Irrigation (hand set)	1900			**9.2**	**5.1**	2
Cotton (AZ and CA)	1	Weeding, Hand	70	1.98	3.55	250	140	0 (12 hours)
		Scouting	210			83	46	0 (12 hours)
Forage Crop (clover grown for seed)	1	Scouting	1100			16	**8.8**	2
		Irrigation (hand set)	1900	1.98	3.55	9.2	**5.1**	2
Onion, bulb (CA, OR, ID, WA)	1	Scouting	330	1.98	3.55	53	29	0 (12 hours)
		Thinning Plants	330			53	29	0 (12 hours)
		Scouting	1400			12	**6.9**	0 (12 hours)
		Weeding, Hand	1400			12	**6.9**	0 (12 hours)
		Irrigation (hand set)	1900			**9.2**	**5.1**	2
		Weeding, Hand	4200			**4.1**	**2.3**	3
Potato (all states)	1	Weeding, Hand	70	1.98	3.55	250	140	0 (12 hours)
		Scouting	210			83	46	0 (12 hours)
		Irrigation (hand set)	1900			**9.2**	**5.1**	2
Cotton [All states (except CA and AZ)]	0.5	Weeding, Hand	70	0.99	1.775	500	280	0 (12 hours)
		Scouting	210			170	93	0 (12 hours)
Onion, bulb (MI, NM, TX)	0.5	Scouting Thinning Plants	330	0.99	1.775	110 110	59 59	0 (12 hours) 0 (12 hours)
		Scouting Weeding, Hand	1400			25 25	14 14	0 (12 hours) 0 (12 hours)
		Irrigation (hand set)	1900			18	10	1
		Weeding, Hand	4200			**8.3**	**4.6**	2
Peanut	0.5	Weeding, Hand	70	0.99	1.775	500	280	0 (12 hours)
		Scouting	210			170	93	0 (12 hours)
		Irrigation (hand set)	1900			18	10	1

Bold MOE values are below the LOC of 100.

a. DFR = residue values from tomato and cucumber DFR studies; adjusted to account for application rate differences.

b. MOE = POD (0.069 mg/kg/day) / Daily Dermal Dose. DAF is 2%.

Table 11.2.2.6. Oxamyl Post-Application Risks for Cotton Harvesting using DBR Data.

Crop	Application rate (lb ai/A)	Activity	Transfer Coefficient (g cotton boll/hr)	DBR (ug/g)[a]		MOE[b]		Day at which MOE ≥10
				Day 0	Day 14 (current PHI)	Day 0	Day 14 (current PHI)	
Cotton	0.5	Module Builder Operator	900	0.384	0.013	100	2900	0 (12 hours)
		Picker Operator and Raker	2,400			37	1100	0 (12 hours)
		Tramper	5,050			18	520	0 (12 hours)
	1	Module Builder Operator	900	0.769	0.026	50	1500	0 (12 hours)
		Picker Operator and Raker	2,400			19	550	0 (12 hours)
		Tramper	5,050			**8.9**	260	1

Bold MOE values are below the LOC of 10.

a. DBR = residue values from tribufos DBR study; adjusted to account for application rate differences.
b. MOE = POD (0.069 mg/kg/day) / Daily Dermal Dose.

Restricted Entry Interval (REI)

Oxamyl is classified as Toxicity Category IV via the dermal route, Toxicity Category III for primary eye irritation, and Toxicity Category IV for dermal irritation potential. It is not a skin sensitizer. There were risk estimates of concern related to certain crop/activity combinations; therefore, HED is recommending that the REI be revised on the label to address those concerns. Both registered product labels currently have REIs of 48 hours; however, based on the current post-application dermal exposure assessment (Tables 10.2.2.2 – 10.2.2.6), REIs of 12 hours to more than 7 days would be necessary to reach acceptable MOEs (i.e., MOEs ≥ 10) from exposure to oxamyl residues.

12.0 Public Health and Pesticide Epidemiology Data

Oxamyl was previously reviewed in 2009 (M. Hawkins and S. Recore, 11/24/2009, D372501). At the time, there were five incidents reported for oxamyl to Main Incident Data System (IDS) from 2002 to November 24, 2009. There were 15 cases reported to NIOSH Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides (1998-2005) involving oxamyl. Upon review of these incidents, it was concluded that "Based on the low severity and low number of incident cases, there does not appear to be a risk concern at this time that would warrant further investigation."

In the current IDS analysis there was one moderate severity incident reported to Main IDS and one minor severity incident reported to Aggregate IDS from January 1, 2012 to April 5, 2017. An updated query of SENSOR-Pesticides, from 2006-2013, identifies eight additional cases involving oxamyl.

Based on the low frequency and severity of oxamyl incidents reported to both IDS and SENSOR-Pesticides, there does not appear to be a concern at this time. The Agency will continue to monitor the incident data and if a concern is triggered, additional analysis will be conducted.

Appendix A. Toxicology Profile and Executive Summaries

A.1 Toxicology Data Requirements

Study requirements (40 CFR §158.500) for oxamyl are presented below. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Study		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity (rat)	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity (rat)	yes	yes
870.2400	Acute Eye Irritation (rabbit)	yes	yes
870.2500	Acute Dermal Irritation	yes	yes
870.2600	Skin Sensitization	yes	yes
870.3100	90-Day Oral Toxicity (rodent)	yes	yes[1]
870.3150	90-Day Oral Toxicity (nonrodent)	yes	yes[2]
870.3200	21/28-Day Dermal Toxicity	yes	yes
870.3250	90-Day Dermal Toxicity	no	--
870.3465	90-Day Inhalation Toxicity (rat)	yes	yes[3]
870.3700a	Prenatal Developmental Toxicity (rodent)	yes	yes
870.3700b	Prenatal Developmental Toxicity (nonrodent)	yes	yes
870.3800	Reproduction and Fertility Effects	yes	yes
870.4100a	Chronic Toxicity (rodent)	yes	yes
870.4100b	Chronic Toxicity (nonrodent)	yes	yes
870.4200a	Carcinogenicity (rat)	yes	yes
870.4200b	Carcinogenicity (mouse)	yes	yes
870.4300	Combined Chronic Toxicity/Carcinogenicity (rat)	yes	yes
870.5100	Mutagenicity—Bacterial Reverse Mutation Test	yes	yes
870.5300	Mutagenicity—Mammalian Cell Gene Mutation Test	yes	yes
870.5xxx	Mutagenicity— Structural Chromosomal Aberrations	yes	yes
870.5xxx	Mutagenicity—Other Genotoxic Effects	yes	yes
870.6200a	Acute Neurotoxicity Screening Battery (rat)	yes	yes
870.6200b	90-Day Neurotoxicity Screening Battery (rat)	yes	yes
870.6300	Developmental Neurotoxicity (rat)	no	-
870.7485	Metabolism and Pharmacokinetics	yes	yes
870.7600	Dermal-penetration	no	yes
870.7800	Immunotoxicity	yes	yes[4]

1 Subchronic exposure in the rat has been evaluated in the prenatal developmental toxicity study, two-generation reproduction toxicity study, and as part of the combined chronic toxicity/carcinogenicity study. Therefore, a study is not required at this time.

2 A subchronic dog study is not needed given a chronic dog study was submitted.

3 A 90-day inhalation toxicity study is not needed based on the rapid recovery of the AChE enzyme (<24 hours). Repeated daily exposure is not expected to result in increased toxicity; and therefore, the available single dose inhalation toxicity study satisfies this requirement.

4 Based on a weight of evidence approach, the Hazard and Science Policy Council (HASPOC) concluded that immunotoxicity study is not required at this time for oxamyl (U. Habiba; 18-JUL-2013; TXR# 0056737).

A.2 Toxicity Profiles

Table A.2.1. Acute Toxicity Profile – Oxamyl.				
Guideline No.	**Study Type**	**MRID(s)**	**Results**	**Toxicity Category**
870.1100	Acute oral	00063011	LD_{50} = 3.1 mg/kg (M); 2.5 mg/kg (F)	I
870.1200	Acute dermal	40606501	LD_{50} > 5000 mg/kg (M) >2000 mg/kg (F)	IV
870.1300	Acute inhalation	00066902	LC_{50} > 0.064 mg/L (4 hr) 0.17 mg/L (M) 0.12 mg/L (F)	II
870.2400	Acute eye irritation	00066894	Marked pupillary constriction, conjunctival irritation, reversible by 7 days.	III
870.2500	Acute dermal irritation	40606501	Mild erythema and edema, cleared by day 5, except in one rabbit that cleared by day 12.	IV
870.2600	Skin sensitization	00066900	4/7 animals died (25% test material) 1/5 animals died (intradermal injection) Effects seen on the test site were slight. Extreme toxicity makes dermal sensitization study relatively unimportant.	Not a skin sensitizer (25% test material)

Table A.2.2. Subchronic, Chronic, and Other Toxicity Profile – Oxamyl.			
Guideline No.	**Study Type**	**MRID No. (year)/ Classification/Doses**	**Results**
870.3100	90-Day Oral Toxicity in Rodents (rat)	NA	NA
870.3150	90-Day Oral Toxicity in Non-Rodents (dog)	NA	NA
870.3200	21/28-Day Dermal Toxicity (rabbit)	40827601 (1988) Acceptable/guideline 0, 2.5, 50, or 250 mg/kg/day	NOAEL = 2.5 mg/kg/day. LOAEL = 50 mg/kg/day based on plasma, RBC, and brain AChE inhibition. No clinical signs were observed.
870.3200	21/28-Day Dermal Toxicity (rabbit)	44751201 (1999) Unacceptable 0, 25, 40, 50, or 75 mg/kg/day	Unacceptable due to surface area treated (1% rather than guideline recommended 10%) and inconsistent water volumes for paste formulation (TXR# 0055349).

Table A.2.2. Subchronic, Chronic, and Other Toxicity Profile – Oxamyl.

Guideline No.	Study Type	MRID No. (year)/ Classification/Doses	Results
870.3700a	Prenatal Developmental in Rodent (rat)	40859201 (1988) Acceptable/guideline 0, 0.2, 0.5, 0.8, or 1.5 mg/kg/day	**Maternal:** NOAEL = 0.5 mg/kg/day. LOAEL = 0.8 mg/kg/day based on decreased bodyweight and food consumption and increased incidence of clinical signs associated with AChE inhibition (increased tremors). **Developmental:** NOAEL = 0.2 mg/kg/day. LOAEL = 0.5 mg/kg/day based on decreased fetal bodyweights
870.3700b	Prenatal Developmental in Non-Rodent (rabbit)	00063009 (1980) Acceptable/guideline 0, 1, 2, or 4 mg/kg/day	**Maternal:** NOAEL = 1 mg/kg/day. LOAEL = 2 mg/kg/day based on decreased bodyweight gains. **Developmental:** NOAEL = 4 mg/kg/day. LOAEL = not established.
870.3800	Reproduction and Fertility Effects (rat)	41660801 (1991) Acceptable/guideline Males: 0, 1.7, 5.2, or 11.6 mg/kg/day Females: 0, 2.0, 6.6, or 15.8 mg/kg/day	**Parental:** NOAEL = 1.7/2.0 [M/F] mg/kg/day. LOAEL = 5.2/6.6 [M/F] mg/kg/day based on decreased food consumption, body weight, and bodyweight gain. At HDT, hyperactivity, skin sores, and alopecia. **Reproductive:** NOAEL = 5.2/6.6 [M/F] mg/kg/day. LOAEL = 11.6/15.8 [M/F] mg/kg/day based on decreased bodyweight during lactation. At HDT, decreased number of live pups per litter during lactation and decreased viability index. **Offspring:** 5.2/6.6 [M/F] mg/kg/day. LOAEL = 11.6/15.8 [M/F] mg/kg/day based on decreased bodyweight during lactation. At HDT, decreased number of live pups per litter during lactation and decreased viability index.
870.4100b	Chronic Toxicity (dog)	41697901, 42052701, 44737503 (1990-1999) Acceptable/guideline Males: 0, 0.372, 0.577, 0.930, 1.364, 1.56, 4.6, or 8 mg/kg/day Females: 0, 1.46, 4.5, or 7.84 mg/kg/day	**Systemic** NOAEL = 1.56/1.46 [M/F] mg/kg/day. LOAEL = 4.6/4.5 mg/kg/day based on decreased bodyweights and bodyweight gains. **Cholinesterase** NOAEL = 0.93/1.56 [M/F] mg/kg/day. LOAEL = 1.36/4.5 [M/F] mg/kg/day based on decreased brain cholinesterase levels in males and vomiting, tremors, plasma and brain AChE inhibition in females.

Table A.2.2. Subchronic, Chronic, and Other Toxicity Profile – Oxamyl.			
Guideline No.	**Study Type**	**MRID No. (year)/ Classification/Doses**	**Results**
870.4200a	Carcinogenicity (rat)	41963201 (1991) Acceptable/guideline Males: 0, 0.992, 1.97, 4.19, or 6.99 mg/kg/day Females: 0, 1.32, 2.69, 6.73, or 11.1 mg/kg/day Only plasma and RBC AChE was measured from 16 hr fasted rats	NOAEL = 1.97/2.69 [M/F]. LOAEL = 4.19/6.73 [M/F] based on hyperactivity, swollen legs/paws, and skin sores, decreased bodyweights and bodyweight gains, increased incidence of ocular findings in males and females and inhibition of plasma AChE in males. No evidence of carcinogenicity.
870.4200b	Carcinogenicity (mouse)	00076813 (1981) Acceptable/guideline 0, 3.75, 7.5, 15/11.25 mg/kg/day	NOAEL = 3.75 mg/kg/day. LOAEL = 7.5 mg/kg/day based on decreased bodyweights in males and mortality in males and females during initial phase of the study. No evidence of carcinogenicity.
870.5100	Gene Mutation *Salmonella typhimurium* reverse gene mutation	40606509 (1981) Acceptable/guideline 50 to 10,00 ug/plate in the +/- of S9 activation	Negative in TA1535, TA1537, TA98, and TA100.
870.5300	Gene Mutation CHO Assay	40606510 (1982) Acceptable/guideline Up to 1200 uM -S9 Up to 700 uM +S9	Negative in trials up to concentrations causing <80% decrease in cell viability (1200 uM -S9; 700 uM +S9).
870.5375	Chromosomal aberration CHO cell chromosomal assay	40606507 (1982) Acceptable/guideline 700 ug/mL +S9 70 ug/mL -S9	Negative up to cytotoxic concentrations (≤70 ug/mL -S9; 700 ug/mL +S9).
870.5500	Bacterial DNA Damage/Repair	00049594 (1976) Acceptable/guideline Up to 2000 ug/disc	Negative up to highest dose tested.
870.5500	Unscheduled DNA synthesis	40606508 and 41096001 (1982) Acceptable/guideline Up to ≤5 mM	Negative up to cytotoxic concentrations.
870.6200a	Acute Neurotoxicity Screening Battery (rat)	44254401, 44420301, 44740701 (1997) Acceptable/guideline Males: 0, 0.1, 1.0, or 2.0 mg/kg/day Females: 0, 0.1, 0.75, or 1.5 mg/kg/day	NOAEL = 0.1 mg/kg/day. LOAEL = 0.75/1.0 [M/F] based on clinical signs, FOB effects, and decreased plasma, RBC, and brain AChE activity.
870.6200b	Subchronic Neurotoxicity Screening Battery (rat)	44504901 (1998) Acceptable/guideline Males: 0, 0.564, 2.10, or 14.9 mg/kg/day Females: 0, 0.679, 2.40, or 19.9 mg/kg/day	NOAEL = 2.10/2.40 [M/F] mg/kg/day. LOAEL = 14.9/19.9 [M/F] mg/kg/day based on plasma, RBC, and brain AChEI.

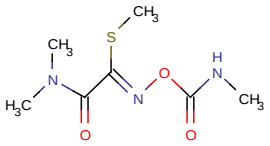
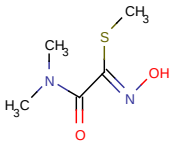
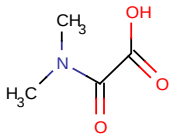
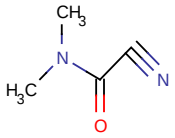
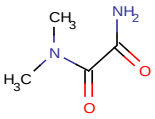
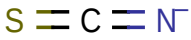
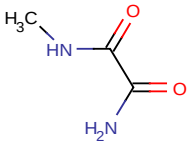
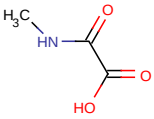
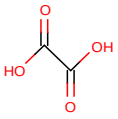
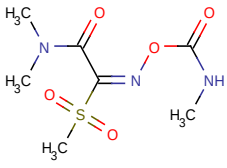
Table A.2.2. Subchronic, Chronic, and Other Toxicity Profile – Oxamyl.			
Guideline No.	**Study Type**	**MRID No. (year)/ Classification/Doses**	**Results**
870.7485	Metabolism and Pharmacokinetics	41520801 (1990) Acceptable/guideline 1 mg/kg	With oral administration, oxamyl was readily absorbed and eliminated in the urin (80-91% of the dose) and feces (<3% of the dose). The major component present in the urine was β-glucuronide of oxime (31-37% of the dose) followed by the metabolite oxime (13-18% of the dose). No tissue accumulation was observed.
870.7600	Dermal Penetration (Rats) *In vivo*	49914102 (2016) -24% ai; 49914104 (2016) - 42% ai Acceptable/guideline 6, 60, or 600 µg/cm^2	Highest absorption at lowest dilution. After 6 hours of exposure, dermal absorption at the lowest dilution was 3-5% (sum of excreta, cage wash, carcass, whole blood, residual feed, non-treated skin, stripped skin, and tape strips excluding strips 1-2) at 144-hours post-dose.
870.7600	Dermal Penetration (Rat and Human Skin) *In vitro*	49914101 (24% ai); 49914103 (42% ai) Acceptable/non-guideline 6, 60, or 600 µg/cm^2	Rat skin more permeable than human skin. At the lowest dilution, 5-6% and 1-2% of administered dose in receptor fluid in rat and human skin, respectively.
Non-guideline	Human Volunteer Study 40 male subjects (ages 19-39)	44912301 (1999) Acceptable/non-guideline Single oral dose: 0, 0.005, 0.015, 0.03, 0.06, 0.09, or 0.15 ai mg/kg	Under the conditions of this ascending oral dose study in humans, 0.09 mg/kg/day represents a level where 7-12% plasma and RBC AChE inhibition was observed. Three of 5 volunteers at this dose (0.09 mg/kg/day) exhibited greater than 20% plasma AChE inhibition. Therefore, 0.06 mg/kg/day is considered the NOAEL. BMD_{10} = 0.083 mg/kg. $BMDL_{10}$ = 0.069 mg/kg.
Non-guideline	Cholinesterase Inhibition Reversibility Study	44472001 (1997) Acceptable/non-guideline 1 mg/kg	Oxamyl technical at 1 mg/kg produced inhibition of plasma, RBC, and brain cholinesterase activities 30 minutes after treatment in male and female rats with complete recovery by 2 hours after treatment, except for female brain cholinesterase activity, which returned to normal levels by 3 hours postdosing.
Non-guideline	Special Acute Inhalation (Rat)	45155801 (2000) Acceptable/non-guideline 0.0049 mg/L or 0.024 mg/L	NOAEL = not established. LOAEL = 0.0049 mg/L based on biologically and statistically significant decreases in plasma, RBC, and brain AChEI in males and females. Brain BMD_{10} = 0.005 mg/kg. Brain $BMDL_{10}$ = 0.004 mg/kg. RBC BMD_{10}= 0.002 mg/L. RBC $BMDL_{10}$= 0.0018 mg/L.

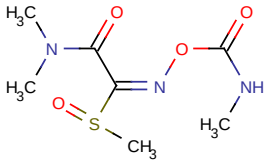
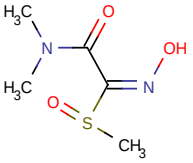
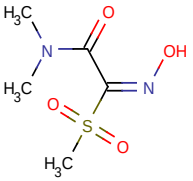
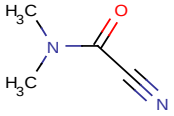
Table A.2.2. Subchronic, Chronic, and Other Toxicity Profile – Oxamyl.			
Guideline No.	**Study Type**	**MRID No. (year)/ Classification/Doses**	**Results**
Non-guideline	Comparative Cholinesterase Assay (Rat)	46615301 (2005) Acceptable/non-guideline 0, 0.15, 0.20, or 0.25 mg/kg	**PND11** NOAEL = not established. LOAEL = 0.075 mg/kg based on RBC AChEI (18% in males, 16% in females) and brain AChEI (11% in males, 7% in females). Brain BMD_{10} = 0.067 mg/kg. Brain $BMDL_{10}$ = 0.043 mg/kg. RBC BMD_{10} = 0.059 mg/kg. RBC $BMDL_{10}$ = 0.039 mg/kg. **Adult** NOAEL = 0.15 mg/kg for brain only (no NOAEL for RBC). LOAEL = 0.15 mg/kg based on RBC AChEI (25% in males, 22% in females) and brain AChEI (10% in males). Brain BMD_{10} = 0.177 mg/kg. Brain $BMDL_{10}$ = 0.145 mg/kg. RBC BMD_{10} = 0.079 mg/kg RBC $BMDL_{10}$ = 0.052 mg/kg.

Appendix B: Physicochemical Properties of Oxamyl

Table B.1. Physicochemical Properties of Technical Grade Oxamyl.		
Parameter	**Value**	**Reference**
Melting range	97-100 °C	Revised Product Chemistry Chapter for the RED; DP# 263858, 3/15/00, K. Dockter
pH	3.4	Oxamyl Reregistration Standard Update; DP#157409, 6/18/91, E. Zager
Density	bulk: 0.34 g/mL absolute: 0.97 g/mL	
Water solubility	28 g/100 g at 25 °C	Revised Product Chemistry Chapter for the RED; DP# 263858, 3/15/00, K. Dockter
Solvent solubility	at 25 °C Methanol 130 g/100 g Acetone 67 g/100 g Ethanol 33 g/100 g Toluene 1 g/100 g	
Vapor pressure	3.84×10^{-7} mm Hg @ 25 ºC	Oxamyl Reregistration Standard Update; DP#157409, 6/18/91, E. Zager
Dissociation constant, pK_a	non-ionic; no acidic or basic properties	
Octanol/water partition coefficient, $Log(K_{OW})$	$K_{ow} = 0.36$ at 25 ºC	
UV/visible absorption spectrum	Not available	

Appendix C: Chemical Names and Structures

Compound	Structure
Oxamyl methyl 2-(dimethylamino)-*N*-[[(methylamino)carbonyl]oxy]-2-oxoethanimidothioate	
Oxime methyl 2-(dimethylamino)-*N*-hydroxy-2-oxoethanimidothioate	
DMOA *N*,*N*-dimethyl-oxalamic acid	
DMCF cyano-methanoic acid dimethylamide	
DMEA *N*,*N*-dimethyl-oxalamide	
thiocyanate	
N-methyloxamide	
N-methyloxamic acid	
oxalic acid	
oxamyl sulfone	

Compound	Structure
oxamyl sulfoxide	
oxime sulfoxide	
oxime sulfone	
N-dimethylcyanoformamide	

Appendix D: Livestock Dietary Burden Calculations

The livestock dietary burdens were calculated in D372355 (3-Aug-2009) and were recalculated to incorporate the most recent guidance (livestock - dietary burden calculator (PMRA ver. 2.8)).

Table D.1. Livestock Dietary Burden Calculations

Crop	Commodity	Type[1]	Residue (ppm)[2]	%Dry Matter	%Diet	Dietary Contribution (ppm)[3]
Beef Cattle						
Cotton	Gin byproducts	R	30.1 (M)	90	5	1.67
Cotton	Hulls	R	0.2 (T)	90	10	0.02
Cotton	Meal	PC	0.2 (T)	89	5	0.01
Untreated feed	not applicable				80	0
Total	**not applicable**				**100**	**1.71**
Dairy Cattle						
Peanut	Hay	R	2 (T)	85	15	0.35
Soybean (should this be deleted)	Hulls	R	0.1 (T)	90	20	0.02
Apples	Pomace, wet	CC	2 (T)	40	10	0.50
Cotton	Undelinted seed	PC	0.2 (T)	88	10	0.02
Untreated feed	not applicable				45	0
Total	**not applicable**				**100**	**0.90**
Poultry						
Cotton	Meal	PC	0.2 (T)	89	20	0.04
Soybean (should this be deleted)	Meal	PC	0.1 (T)	92	5	0.005
Untreated feed	not applicable				75	0
Total	**not applicable**				**100**	**0.05**
Swine						
Cotton	Meal	PC	0.2 (T)	89	15	0.03
Untreated feed	not applicable				85	0
Total	**not applicable**				**100**	**0.03**

[1] R = roughage; PC = protein concentrate; CC = carbohydrate concentrate.
[2] M= median; T = tolerance.
[3] Dietary Contribution = (residue) x (% diet) ÷ (% dry matter); for poultry and swine, % dry matter is not considered.

Appendix E: IRL Sheet

Summary of U.S. Tolerances and International MRLs.

Residue Definition:

U.S.	Canada	Mexico[1]	Codex
40 CFR §180.303(a) tolerances are established for oxamyl (methyl *N*,*N*-dimethyl-*N*-[(methylcarbamoyl)-oxy]-1-thiooxamimidate) and its oxime metabolite (methyl *N*,*N*-dimethyl-*N*-hydroxy-1-thiooxamimidate) calculated as oxamyl in or on the following food commodities:	oxamyl and oxamyl oxime	oxamyl	oxamyl and oxamyl oxime expressed as oxamyl

Commodity Tolerance/Maximum Residue Limit (mg/kg)

Commodity	U.S.	Canada	Mexico[1]	Codex
Apple	2.0	--	--	--
Banana	0.30	--	--	--
Cantaloupe	2.0	--	--	2 (melons other than watermelon)
Carrot	0.10	--	--	0.1
Celery	10	--	3	--
Cotton, undelinted seed	0.20	--	--	0.2
Cotton, gin byproduct	120	--	--	--
Cucumber	2.0	--	--	2
Eggplant	2.0	--	--	--
Fruit, citrus, group 10-10	3.0	--	--	5
Garlic, bulb	0.20	--	--	--
Ginger	0.10	--	--	0.05
Melon, honeydew	2.0	--	--	2 (melons other than watermelon)
Onion, bulb	0.20	--	--	--
Peanut	0.05	--	--	0.05
Peanut, hay	2.0	--	--	--
Pear	2.0	--	--	--
Peppermint, tops	10	--	--	--
Pepper, bell	2.0	--	3	2
Pepper, nonbell	5.0	--	3	--
Pineapple	1.0	--	--	--
Pineapple, process residue	2.0	--	--	--
Potato	0.10	0.1	--	0.1
Pumpkin	2.0	--	--	--
Spearmint, tops	10	--	--	--
Squash, summer	2.0	--	--	--
Squash, winter	2.0	--	--	--
Sweet potato	0.10	--	--	--
Tomato	2.0	--	--	2
Watermelon	2.0	--	--	--
Yam	0.10	--	--	--
Edible offal of cattle, goat, hog, horse, sheep	--	--	--	0.02
Eggs	--	--	--	0.02
Meat (from mammals other than marine mammals)	--	--	--	0.02
Melon	--	--	2	--
Melon (except watermelon)	--	--	--	2
Milk	--	--	--	0.02
Poultry, meat	--	--	--	0.02
Poultry, edible offal of	--	--	--	0.02
Spices, fruit and berries	--	--	--	0.07
Spice, roots and rhizomes	--	--	--	0.05

[1] In general, Mexico adopts U.S. tolerances; the listed Mexican tolerances are those that are different from the U.S.

Appendix F: Registered Formulations and Application Scenarios.

Table F.1. Registered Formulations.

Product Type	Trade Names (EPA Reg. No.)	Conc.	Application Type; Equipment	REI	Target Pests
water soluble liquid	DuPont™ Vydate® C-LV (EPA Reg. No. 352-532)	3.77 lb ai/gallon	broadcast spray; ground, aerial, or chemigation equipment	48 hours	variety of insects, mites, and nematodes
water soluble liquid	DuPont™ Vydate® L (EPA Reg. No. 352-372)	2 lbs ai/gallon	broadcast spray; ground, aerial, chemigation, soil injection	48 hours	

Table F.2. Registered Application Scenarios.

Crop	Label	Geographic Location	Target / Timing	Application Equipment	Maximum Single Application Rate	Restrictions
Apples	352-372	All states	Timing depends on pest; Foliage	Chemigation, Ground (airblast), Handheld	8 pt/A = 2 lb ai/A 50 gal/A = 0.04 lb ai/gal	•Do not apply at bloom or within 30 days after bloom •Min. RTI = 7 days •No more than 4 apps/season •max seasonal rate = 2 lb ai/acre •PHI = 14 days
		Washington		Aerial	4 pt/A = 1 lb ai/A	
		NJ, PA, VA, WV	Thinning; Foliage	Chemigation, Ground (airblast), Handheld	4 pt/A = 1 lb ai/A 2 pt/100 gal = 0.005 lb ai/gal	•Min. RTI = 5 days •No more than 4 apps/season; max seasonal rate = 2 lb ai/acre •PHI = NA
Bananas, Plantains	352-372	Puerto Rico	Foliage / Soil Planting / Post-planting	Manually-pressurized handwand	10 mL / plant = 0.005 lb ai/plant	•Min. RTI = 21 days •No more than 4 apps/season •max yearly rate = 4 lb ai/acre •PHI = 1 day
			Foliage / Soil New & Existing Plantings	Chemigation	2/3 gal/A = 1.34 lb ai/A	
Carrot (not registered in CA)	352-372	AR, CO, IA, IL, KS, LA, MN, MO, MS, MT, ND, NE, OK, SD, TN, TX (except the Rio Grande Valley), WI, and WY	Pre-plant / Soil Pre-emergence In-furrow treatment (apply in seed furrow during planting) Soil directed (must be incorporated by water or mechanical means to at least 2 in deep)	Groundboom, Chemigation	1 gal/A = 2 lb ai/A	•Min. RTI = 14 days •No more than 3 soil-directed post-emergence apps per season (or 4 total apps including a preplant app) •Apply within 1 week of planting if applied pre-plant or before emergence if post-plant •max seasonal rate = 5 lb ai/acre •PHI = 14 days
		All other states and the Rio Grande Valley in TX			2 gal/A = 4 lb ai/A	•Min. RTI = 14 days •No more than 8 apps per season •max seasonal rate = 8 lb ai/acre •PHI – 14 days

Table F.2. Registered Application Scenarios.

Crop	Label	Geographic Location	Target / Timing	Application Equipment	Maximum Single Application Rate	Restrictions
Celery	352-372	MI, OH, PA, TX (except the Rio Grande Valley)	Transplant Treatment Pre-plant Row Soil Treatment Foliar Treatment	Groundboom, Chemigation	Soil directed: 1 gal/A = 2 lb ai/A (100 gal/A = 0.02 lb ai/gal) Foliar directed: 4 pt/A = 1 lb ai/A (20 gal/A = 0.05 lb ai/gal)	•Min. RTI = 14 days •No more than 4 foliar apps per season (5 total apps including a transplant or preplant app) •Soil apps must be incorporated •max seasonal rate = 6 lb ai/acre •PHI = 21 days
		AZ, CA, FL	Foliar	Aerial, Chemigation and Groundboom	4 pt/A = 1 lb aiA	•Min. RTI = 5 days •No more than 8 apps per season •Soil apps must be incorporated •max seasonal rate = 6 lb ai/acre •PHI = 21 days
		FL and Rio Grande Valley of TX	Transplant treatment Foliar Preplant Row Soil treatment	Groundboom, Chemigation	Foliar: 1 gal/A = 2 lb ai/A Soil directed: 2 gal/A = 4 lb ai/A	
		CA	Band Treatment or soil injection	Groundboom, Chemigation	4 pt/A = 1 lb ai/A	
Citrus	352-372	All states	Foliar	Aerial, Ground (airblast), Chemigation, Handgun	4 pt/A = 1 lb ai/A 1 pt/100 gal = 0.0025 lb ai/gal	•Min. RTI = 14 days •No more than 6 apps per year •Soil apps must be incorporated •max yearly rate = 6 lb ai/acre •PHI = 7 days
		CA	Soil	Chemigation	8 pt/A = 2 lb ai/A	•Min. RTI = 30 days at max rate •max yearly rate = 6 lb ai/acre •PHI = 7 days
		FL				
Cotton	352-532	All states (except CA and AZ)	Make apps when damaging populations begin to build	Aerial, Chemigation and Groundboom	17 fl oz/A = 0.5 lb ai/A	•Min. RTI = 7 days •max seasonal rate = 3 lb ai/acre •PHI = 14 days •Apps by handwand or soil broadcast are prohibited •Do not make more than 4 or 8 apps per season depending on location (specific states noted in label)
		AZ			34 fl oz/A = 1 lb ai/A	•Min. RTI = 6 days; max 8 apps/season •max seasonal rate = 3 lb ai/acre •PHI = 14 days •Apps by handwand or soil broadcast are prohibited
		CA				

Table F.2. Registered Application Scenarios.

Crop	Label	Geographic Location	Target / Timing	Application Equipment	Maximum Single Application Rate	Restrictions
Cucumber, Cantaloupe, Honeydew Melon, Watermelon, Squash, Pumpkin	352-372	AL, FL, GA, MS, NC, SC, and TX (except the Rio Grande Valley)	Preplant and Planting Soil Treatment Foliar treatment Chemigation and Soil injection systems	Aerial, Chemigation and Groundboom	Soil: 1 gal/A = 2 lb ai/A Foliar/Chemigation: 4 pt/A = 1 lb ai/A Chemigation:	•Min. RTI = 7 days •3 to 4 apps allowed per season depending on the preplant/at plant app rate •Soil injection must be at least 2 in deep •max seasonal rate = 4 lb ai/acre •PHI – 1 day
		All other states and the Rio Grande Valley of TX			Soil: 2 gal/A = 4 lb ai/A Foliar/Chemigation: 4 pt/A = 1 lb ai/A	•Min. RTI = 7 days •No more than 8 apps per season •max seasonal rate = 6 lb ai/acre •PHI = 1 day
Eggplant	352-372	AL, CO, FL, GA, IA, IL, IN, KY, MI, MN, MO, MS, NC, ND, NE, OG, SC, SD, TN, WI, WV, WY	Foliar: When insects appear Soil: 2-3 weeks after transplanting Soil injection/Chemigation: either at time of transplanting or within 14 days	Groundboom / Chemigation	4 pt/A = 1 lb ai/A	•Min. RTI = 10 days •No more than 4 foliar, drip, or soil injection apps/season (or 6 including 2 postplant soil treatments) •Soil apps must be at least 2 in deep •max seasonal rate = 4 lb ai/acre •PHI = 1 – 7 days depending on pest
		AR, KS, LA, OK, and TX (except the Rio Grande Valley of TX)				•Min. RTI = 10 days •No more than 3 foliar, drip, or soil injection apps/season •Soil apps must be at least 2 in. deep •max seasonal rate = 3 lb ai/acre •PHI = 1 – 7 days depending on pest
		All other states and the Rio Grande Valley of TX)			Foliar/Chemigation/Soil Injection: 4 pt/A = 1 lb ai/A Soil treatment: 1 gal/A = 2 lb ai/A	•Min. RTI = 7 days •No more than 8 apps/season •Soil apps must be at least 2 in deep •max seasonal rate = 6 lb ai/acre •PHI = 1 – 7 days depending on pest
Garlic	352-372	OR and CA	Before population starts to build	Aerial, Groundboom, Chemigation	4 pt/A = 1 lb ai/A	•Min. RTI = 7 days •No more than 8 apps/season

Table F.2. Registered Application Scenarios.

Crop	Label	Geographic Location	Target / Timing	Application Equipment	Maximum Single Application Rate	Restrictions
		CA	At planting or post-emergence	Aerial, Groundboom or Chemigation	Soil: 1 gal/A = 2 lb ai/A At planting (ground): 2 gal/A = 4 lb ai/A Postemergence (ground): 1 gal/A = 2 lb ai/A Postemergence (air): ½ gal/A = 1 lb ai/A	•Soil apps must be incorporated into soil by water or mechanical means •max seasonal rate = 4.5 lb ai/acre •PHI = 14 days
		OR				
Ginger Root	352-372	HI only	Pre-plant soil treatment	Groundboom	2 gal/A = 4 lb ai/A	•Min. RTI = 30 days •No more than 8 apps/season •Do not apply by chemigation •max seasonal rate = 10 lb ai/acre •PHI = 30 days
			Post-plant treatment		4 pt/A = 1 lb ai/A	
Nonbearing Fruit (apple, cherry, citrus, peach, pear)	352-372	AL, FL, GA, IN, KY, MS, NC, OH, SC, TX (except the Rio Grande Valley of TX), WV	Foliar when insect infestation high Preplant soil incorporated: within 24 hours before transplanting	Aerial, Chemigation and Groundboom	Foliar: 4 pt/A = 1 lb ai/A Soil: 1 gal/A = 2 lb ai/A	•Nonbearing trees will not bear fruit within 12 months after application •Min. RTI = 14 days •No more than 5 foliar apps/season (or 6 total apps including a preplant app) •max seasonal rate = 7 lb ai/acre •PHI = NA
		AR, KS, and OK				•No more than 3 foliar apps/season (or 4 total apps including a preplant app) •max seasonal rate = 5 lb ai/acre
		All other states and the Rio Grande Valley of TX			Foliar: 84 pt/A = 2lb ai/A Soil: 1 gal/A = 2 lb ai/A	•Min. RTI = 7 days •No more than 8 apps •max seasonal rate = 8 lb ai/acre
Onions (dry bulb only)	352-372	MI, NM, TX	Apply when populations begin to build	Aerial, Chemigation, Groundboom	2 pt/A = 0.5 lb ai/A	•Min. RTI = 5 days •No more than 8 apps •Do not harvest tops of treated onions •Do not use on green onions •max seasonal rate = 4.5 lb ai/acre •PHI = 14 days •Soil apps must be made at least 2 in deep, and incorporated by
		CA, OR, ID, WA			4 pt/A = 1 lb ai/A	
		MI and TX	At planting or postemergence	Groundboom or Chemigation	2 gal/A = 4 lb ai/A	
		ID, OR, WA		Aerial, Groundboom, Chemigation	At planting soil: 2 gal/A = 4 lb ai/A Postemerg. (ground): 1 gal/A = 2 lb ai/A	

Table F.2. Registered Application Scenarios.

Crop	Label	Geographic Location	Target / Timing	Application Equipment	Maximum Single Application Rate	Restrictions
					Postemerg. (air): ½ gal/A = 1 lb ai/A	water or mechanical means
		CA		Groundboom or Chemigation	1 gal/A = 2 lb ai/A	
	NV-070002	NV	At planting or postemergence	Aerial, Groundboom, Chemigation	2 gal/A = 4 lb ai/A Postemergence: 8 pt/A = 1 lb ai/A	
Peanuts (not registered in CA)	352-532	All states (except CA)	At plant soil	Groundboom, Chemigation	68 fl oz/A = 2 lb ai/A	•Min. RTI = 14 days •No more than 5 apps •max seasonal rate = 4 lb ai/acre •PHI = not stated
			Foliar following soil fumigation, pre-plant or at planting soil apps	Aerial, Groundboom, Chemigation	17 fl oz/A = 0.5 lb ai/A	
Pears	352-372	All states (except CA)	Foliar Apply when mites first appear	Ground (airblast), Chemigation	8 pt/A = 2 lb ai/A	•Do not apply at bloom or within 30 0days after full bloom •Do not make more than 1 apap/season •max seasonal rate = 2 lb ai/acre •PHI = 14 days •Use ground equipment only
Peppermint and Spearmint	352-372	ID, MI, MT, OR, WA, and WI only	Apply as mint beaks winter dormancy and begins active root growth	Aerial, Groundboom, Chemigation	Aerial: ½ gal/A = 1 lb ai/A Ground: 1 gal/A = 2 lb ai/A	•Min. RTI = 21 days •max seasonal rate = 4 lb ai/acre •PHI = 21 days •Do not make more than 2 apps/season •Incorporate into soil as soon as possible
Peppers (Bell and Non-Bell)	352-372	AR, KS, LA, MS, OK, and TX (except the Rio Grande Valley)	Transplant water treatment (during transplant) Foliar/Chemigation (14 days after transplant)	Aerial, Chemigation, Groundboom	2 pt/A = 0.5 lb ai/A	•Min. RTI = 10 days •max seasonal rate = 3 lb ai/acre •PHI = 7 days •Do not make more than 4 post-transplant apps per season (5 total including a transplant app) •Soil apps must be at least 2 in deep
		NM and Rio Grande Valley of TX	Soil Injection (when insects first appear)			•Min. RTI = 7 days •max seasonal rate = 3.5 lb ai/acre •PHI = 7 days •Do not make more than 5 post-transplant apps per season (6 total including a transplant app)

Table F.2. Registered Application Scenarios.

Crop	Label	Geographic Location	Target / Timing	Application Equipment	Maximum Single Application Rate	Restrictions
						•Soil apps must be at least 2 in deep
		All other states			4 pt/A = 1 lb ai/A	•Min. RTI = 7 days •max seasonal rate = 6 lb ai/acre •PHI = 7 days •Do not make more than 8 apps per season •Soil apps must be at least 2 in deep
Pineapple	352-372	All states except CA	Planting treatment: Apply within 1 week of planting Foliar/Chemigation: being when pineapple roots begin to grow	Groundboom, Chemigation	1 gal/A = 2 lb ai/A	•Min. RTI = 14 days •max seasonal rate = 8 lb ai/acre •PHI = 30 days •Do not make more than 8 apps per season
Potatoes	352-532	AL, AZ, FL, GA, KS, LA, MS, NC, OK, SC, and TX (Except Rio Grande Valley)	Foliar and Soil – apply when insects appear	Aerial, Groundboom, Chemigation	Foliar: 34 fl oz/A = 1 lb ai/A Soil: 68 fl oz/A = 2 lb ai/A	•Min. RTI = 14 days •max seasonal rate = 6 lb ai/acre •PHI = 7 days •Do not make more than 4 apps per season (depending on location noted in label)
		All states except those listed above				•Min. RTI = 5 days •max seasonal rate = 9 lb ai/acre •PHI = 7 days •Do not make more than 8 apps per season
	PA-070002	PA	Foliar In-furrow application	Groundboom, Chemigation	4.2 pt/A = 2 lb ai/A	•Min. RTI = 14 days; max 8 apps/season •max seasonal rate = 6 lb ai/acre •PHI = 7 days
Sweet Potatoes	352-372	All states except CA	Preplant soil treatment (apply within 1 week of planting) In furrow soil treatment (apply during planting of slips)	Groundboom, Chemigation	2 gal/A = 4 lb ai/A	•Min. RTI = not stated •max seasonal rate = 6 lb ai/acre PHI = not stated
Tobacco	352-532	All states	Soil treatment Row treatment Broadcast and Bed treatment	Groundboom, Chemigation	68 fl oz/A = 2 lb ai/A	•Min. RTI = not stated •max seasonal rate = 2 lb ai/acre •PHI = not stated •Do not make more than 1 apps per season at the max rate
Tomatoes	352-372	AL, AR, DE, FL, GA, IA, IL, IN, KY,	Chemigation / Soil at plant and	Aerial,	4 pt/A = 1 lb ai/A	•Min. RTI = 7 days

Table F.2. Registered Application Scenarios.

Crop	Label	Geographic Location	Target / Timing	Application Equipment	Maximum Single Application Rate	Restrictions
		LA, LA, MD, MI, MN, MS, NC, NJ, NY, OH, PA, SC, TN, TX (except the Rio Grande Valley), VA, WI, WV	transplant / Foliar / Soil injection	Groundboom, Chemigation		• max seasonal rate = 8 lb ai/acre • PHI = 3 days • Do not make more than 7 foliar, drip, or soil apps per season (8 total apps including a soil at plant/transplant app)
		All other states and the Rio Grande Valley			Soil injection: 5 pt/A = 1.25 lb ai/A Chemigation: 8 pt/A = 2 lb ai/A Foliar/Soil at plant and transplant: 4 pt/A = 1 lb ai/A	• Min. RTI = 5 days • max seasonal rate = 8 lb ai/acre • PHI = 3 days • Do not make more than 8 apps per season
Yams	352-372	Puerto Rico only	Foliar after soil fumigation or following pre-plant or at planting soil application of other nematicides	Groundboom	2 pt/A = 0.5 lb ai/A	• Min. RTI = 14 days • max seasonal rate = 4 lb ai/acre • PHI = 60 days • Do not make more than 8 apps per season