

Mandipropamid
PC Code: 036602

Risk Assessment Document

DP Number: 374096



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

MEMORANDUM

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Date: 27-April-2010

SUBJECT: Mandipropamid; Human Health Risk Assessment for the Section 18 Use on Basil.

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Petition No.: 09IL01
Risk Assessment Type: Single Chemical, Aggregate
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Case No.: NA
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FROM: Roger Chesser, Biologist
ARIA/RIMUERB/RD (7505P)

THROUGH: Breann Hanson, Biologist
ARIA/RIMUERB/RD (7505P)

Michael A. Doherty, Ph.D., Chemist
Registration Action Branch 2 (RAB2)
Health Effects Division (HED; 7509P)

TO: Barbara Madden
ARIA/RIMUERB/RD (7505P)

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Mandipropamid

Risk Assessment Document

DP Num: 374096

Table of Contents

1.0 Executive Summary 3

2.0 Ingredient Profile 4

2.1 Structure and Nomenclature 4

2.2 Physical and Chemical Properties 5

2.3 Summary of Proposed Uses 5

3.0 Hazard Characterization/Assessment 6

3.1 Endocrine Disruption 7

4.0 Public Health and Pesticide Epidemiology Data 8

5.0 Dietary Exposure/Risk Characterization 8

5.1 Pesticide Residue Profile 8

5.2 Dietary Exposure and Risk 10

6.0 Residential and Other Exposures (Spray Drift, etc.) 11

7.0 Aggregate Risk Assessments and Risk Characterization 12

8.0 Cumulative Risk Characterization/Assessment 12

9.0 Occupational Exposure/Risk Pathway 12

9.1 Short-/Intermediate-Term Occupational Handler Risk 13

9.2 Short-/Intermediate-Term Occupational Post-application Risk 13

10.0 References: 14

Appendix A: Tolerance Setting 15

Appendix B: Review of Human Research 15

Mandipropamid

Risk Assessment Document

DP Num: 374096

1.0 Executive Summary

The Illinois Department of Agriculture has declared a crisis Section 18 exemption allowing the use of mandipropamid (as Revus™ Fungicide, EPA Reg. No. 100-1254) on basil to control downy mildew. Basil is harvested many times during the season, and the use of Revus™ Fungicide will extend the growing season until the first frost, approximately six additional weeks. The previous risk assessment conducted for mandipropamid was completed in conjunction with its registration for use on tobacco (DP Num; 365919, D. Rate, 8/JUL/2009).

Mandipropamid is a fungicide in the mandelamide class developed by Syngenta Crop Protection, Inc. for the control of foliar oomycete pathogens in a range of crops including *Plasmopara viticola* in grapes, *Phytophthora infestans* in potatoes and tomatoes, and *Pseudoperonospora cubensis* in cucurbits.

The product requested for emergency use is Revus™ Fungicide (EPA Reg. No. 100-1254). The use pattern summary is taken from draft Section 18 labeling and the Revus™ product label. Revus is a liquid formulation which contains 2.08 lb ai (23.3%) mandipropamid per gallon. The product is proposed for multiple foliar applications using ground, chemigation, or aerial equipment at a maximum seasonal rate of 32 fluid oz formulation/A/season or 4 applications/A/season at the maximum rate of application. The proposed preharvest interval (PHI) is 7 days.

For the purposes of this Section 18, the toxicology data base is adequate. Mandipropamid has low or minimal acute toxicity via the oral (Category IV), dermal (Category IV), and inhalation routes of exposure (Category IV). It is minimally irritating to the eye (Category IV), non-irritating to the skin (Category IV) and is negative for skin sensitization. Liver toxicity was the primary effect and was observed in rats, mice and dogs. There was no evidence of increased neonatal sensitivity in the developmental and reproduction toxicity studies, and no evidence of developmental effects, neurotoxicity, mutagenicity or carcinogenicity after exposure to mandipropamid. The FQPA Safety Factor (SF) has been reduced to 1X.

Based on the available data, there are no effects attributable to a 1-day exposure to mandipropamid which are appropriate for assessing acute risks. Similarly, there are no effects attributable to dermal exposure. Therefore, only inhalation and chronic dietary points of departure have been selected.

No data depicting residues of mandipropamid in/on basil are available at this time. ARIA translated residue data from vegetables, leafy (Crop Group 4) to derive an appropriate tolerance level for basil, fresh, and used maximum theoretical concentration factors (12X) for recommending a conservative tolerance for basil, dried.

A screening-level dietary assessment (food + drinking water), based on tolerance-level residues and 100% of crops treated, indicates that chronic dietary risks are below OPP's level of concern for all population subgroups. There are no uses of mandipropamid that would result in residential exposure that OPP can assess; therefore, there are no aggregate risks of concern

Mandipropamid

Risk Assessment Document

DP Num: 374096

either. Occupational risk estimates associated with this emergency exemption are also below OPP's level of concern.

No risks of concern have been identified for the emergency exemption use of mandipropamid on basil; therefore, ARIA recommends for granting the exemption and establishing time-limited tolerances for residues of mandipropamid in/on basil, fresh at 20 ppm and basil, dried at 240 ppm.

Environmental Justice

Potential areas of environmental justice concern, 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," (<http://homer.ornl.gov/nuclearsafety/nsea/oepa/guidance/justice/eo12898.pdf>).

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 (as it relates to an imported crop), ARIA estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food consumption. Extensive data on food consumption patterns are compiled by the USDA under the Continuing Survey of Food Intake by Individuals (CSFII) and are used in pesticide risk assessments for all proposed/registered food uses/tolerances of a pesticide. These data are analyzed and categorized by subgroups based on age, season of the year, ethnic group, and region of the country. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure from traditional dietary patterns among specific subgroups.

Human Data

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 studies (listed in Appendix B) have been determined to require a review of their ethical conduct, and have received that review.

2.0 Ingredient Profile

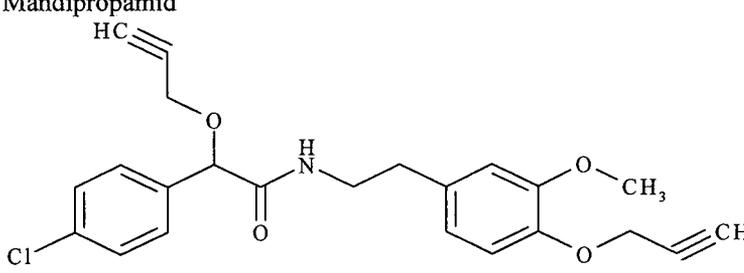
The chemical structure and nomenclature of mandipropamid are presented in Table 2.1. The physicochemical properties of the technical grade mandipropamid are presented in Table 2.2. Mandipropamid is a fungicide in the mandelamide class developed by Syngenta Crop Protection, Inc. for the control of foliar oomycete pathogens in a range of crops. A summary of the proposed uses is presented in Table 2.3.

2.1 Structure and Nomenclature

Mandipropamid

Risk Assessment Document

DP Num: 374096

Table 2.1. Test Compound Nomenclature.	
Compound	
Common name	Mandipropamid 
Company experimental name	NOA 446510
IUPAC name	(<i>RS</i>)-2-(4-chloro-phenyl)- <i>N</i> -[2-(3-methoxy-4-prop-2-ynyloxy-phenyl)-ethyl]-2-prop-2-ynyloxy-acetamide
CAS name	4-chloro- <i>N</i> -[2-[3-methoxy-4-(2-propynyloxy)phenyl]ethyl]- α -(2-propynyloxy)-benzeneacetamide
CAS registry number	374726-62-2
End-use product (EP)	Revus™ (2.08 lb/gal; EPA Reg. No. 100-1254), (Alternate Brand Name: Mandy Flowable Fungicide)

2.2 Physical and Chemical Properties

Table 2.2. Physical and chemical Properties of the Technical Grade of Mandipropamid.		
Parameter	Value	Reference
Melting point/range	96.4-97.3°C	MRID 46800006 (100-REIR.doc, S. Mathur, 22/MAY/2007)
Molecular formula/weight	C ₂₃ H ₂₂ ClNO ₄ / 411.9	
pH	6-8 at 25°C (1% aqueous dispersion)	
Density	1.24 x 10 ³ kg/m ³ at 22°C	
Water solubility (25°C)	4.2 mg/L	
Solvent solubility (25°C)	n-hexane 42 mg/L n-octanol 4.8 g/L toluene 29 g/L methanol 66 g/L ethyl acetate 120 g/L acetone 300 g/L dichloromethane 400 g/L	
Vapor pressure	<9.4 x 10 ⁻⁷ Pa at 25°C or <7.0 x 10 ⁻⁹ mmHg	
Dissociation constant, pK _a	No dissociation constant in the pH range of 1 to 12	
Octanol/water partition coefficient, Log(P _{ow})	3.3 at 25°C	

2.3 Summary of Proposed Uses

Table 2.3. Details of Proposed Uses of 2.08 lb ai/gal FIC (Revus™) on Basil.				
Application Timing, Type, and Equipment	Maximum Single Application Rate (lb ai/A)	Maximum Number of Applications per Season	Maximum Seasonal Application Rate (lb ai/A)	PHI (days)

Mandipropamid

Risk Assessment Document

DP Num: 374096

Table 2.3. Details of Proposed Uses of 2.08 lb ai/gal FIC (Revus™) on Basil.				
Application Timing, Type, and Equipment	Maximum Single Application Rate (lb ai/A)	Maximum Number of Applications per Season	Maximum Seasonal Application Rate (lb ai/A)	PHI (days)
Basil				
	0.13	4	0.52	7
Postemergence Foliar spray Ground, aerial, or Chemigation	Use Directions and Restrictions: Begin applications prior to disease development and continue throughout the season on a 7-10 day interval. Make no more than 2 consecutive applications before switching to an effective non-Group 40 fungicide. May be tank mixed with another fungicide labeled for downy mildew that has a different mode of action. The addition of a spreading/penetrating type adjuvant such as a non-ionic based surfactant or blend may improve activity.			

The supplemental label for Revus™ is adequate to allow evaluation of the residue data relative to the proposed uses on basil.

3.0 Hazard Characterization/Assessment

No changes have been made in the ingredient profile of mandipropamid since the previous risk assessment. Please refer to the previous risk assessment for detailed hazard characterization for mandipropamid (DP Num; 365919, D. Rate, 8/JUL/2009).

HED previously recommended that the FQPA Safety Factor (SF) be reduced to 1X because there is no evidence of increased susceptibility, there are no/low concerns and no residual uncertainties regarding pre- and/or postnatal toxicity, there is no evidence of neurotoxicity in the database and a DNT study is not required. Although the data base is missing the immunotoxicity study as per the revised 40 CFR§158 (FR/Vol. 72, No. 207), the toxicological database is adequate for risk assessment and based on available toxicity data, there is no need for an additional uncertainty factor while the immunotoxicity study is completed. The overall weight of evidence in terms of hematology, clinical chemistry, organ weights, and/or histopathology suggests that mandipropamid does not directly target the immune system. Therefore ARIA does not believe that conducting a functional immunotoxicity study will result in a lower point of departure (POD) than currently selected for overall risk assessment, and therefore, a database uncertainty factor (UF_{DB}) is not needed to account for the lack of this study. Furthermore, the exposure assessments are based on reliable data and reasonable worst-case assumptions and will not likely underestimate risks.

Table 3.1a Toxicological Doses and Endpoints for Mandipropamid for Use in Dietary and Non-Occupational Human Health Risk Assessments				
Exposure/ Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General Population, including Infants and Children)	N/A	N/A	N/A	<u>No appropriate endpoint was identified, and a risk assessment was not conducted.</u>

Mandipropamid

Risk Assessment Document

DP Num: 374096

Table 3.1a Toxicological Doses and Endpoints for Mandipropamid for Use in Dietary and Non-Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (Females 13-49 years of age)	N/A	N/A	N/A	<u>No appropriate endpoint was identified, and a risk assessment was not conducted.</u>
Chronic Dietary (All Populations)	NOAEL = 5 mg/kg/day	UF _A = 10X UF _H = 10X FQPA SF = 1X	Chronic RfD = 0.05 mg/kg/day cPAD = 0.05 mg/kg/day	<u>Chronic toxicity – dogs</u> LOAEL = 40 mg/kg/day, based on evidence of liver toxicity (increased incidence and severity of microscopic pigment in the liver and increased alkaline phosphatase activity in both sexes as well as increased alanine aminotransferase activity in males).
Cancer (oral, dermal, inhalation)	“Not Likely to be Carcinogenic to Humans.” No treatment-related tumors observed in carcinogenicity studies in rats and mice. A cancer risk assessment was not conducted, the chronic risk assessment would be protective of any cancer effects.			

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). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (c = chronic). RfD = reference dose. N/A = not applicable.

Table 3.1b Summary of Toxicological Doses and Endpoints for Mandipropamid for Use in Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal (1-30 days) and Intermediate-term (1-6 months)	N/A	N/A	N/A	<u>No appropriate endpoint was identified, and a risk assessment was not conducted.</u> 28-day dermal toxicity study – rat, no systemic or dermal effect up to the limit dose of 1000 mg/kg/day; there were no neurotoxicity or developmental concerns.
Inhalation Short-(1-30 days) and Intermediate-term (1-6 months)	NOAEL = 41 mg/kg/day IAF=100%	UF _A = 10X UF _H = 10X	Residential LOC for MOE = 100	<u>90-day oral toxicity – rats</u> LOAEL = 260 mg/kg/day, based on decreased body weights, body weight gains and food utilization in males and slight hepatotoxicity in both sexes.
Cancer (oral, dermal, inhalation)	“Not Likely to be Carcinogenic to Humans.” No treatment-related tumors observed in carcinogenicity studies in rats and mice. A cancer risk assessment was not conducted, the chronic risk assessment would be protective of any cancer effects.			

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 (intra-species). MOE = margin of exposure. LOC = level of concern. N/A = not applicable. IAF=inhalation absorption factor.

3.1 Endocrine Disruption

As required under FFDCA section 408(p), EPA has developed the Endocrine Disruptor Screening Program (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

Mandipropamid

Risk Assessment Document

DP Num: 374096

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.

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. This list of chemicals was selected based on the potential for human exposure through pathways such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

Mandipropamid is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Under FFDCA sec. 408(p) the Agency must screen all pesticide chemicals. Accordingly, EPA anticipates issuing future EDSP test orders/data call-ins for all pesticide active ingredients.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, the test guidelines and the Tier 1 screening battery, please visit our website: <http://www.epa.gov/endo/>.

4.0 Public Health and Pesticide Epidemiology Data

Based on the recent registration of this chemical, usage patterns and the lack of residential use sites, no incident reports are expected at this time. Additionally, no public health or epidemiology data were found for this chemical when searched in the National Library of Medicine TOXNET databases.

5.0 Dietary Exposure/Risk Characterization

5.1 Pesticide Residue Profile

The nature of the residue for mandipropamid is adequately understood for purposes of tolerance enforcement and risk assessment, and the residues of concern are summarized in Table 5.1.1. A tolerance-enforcement method, based on the German Multi-residue Method DFG S-19, is available and has been validated for a number of plant commodities. The method is expected to be suitable for analysis of basil.

Table 5.1.1. Summary of Metabolites and Degradates to be Included in the Risk Assessment and Tolerance Expression.

Mandipropamid Risk Assessment Document DP Num: 374096

Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop	Parent mandipropamid (Parent + SYN 500003 for root and tuber vegetables)	Parent mandipropamid
	Rotational Crop	Not applicable	Parent mandipropamid*
Livestock	Ruminant	Not applicable	Not applicable
	Poultry	Not applicable	Not applicable
Drinking Water		Parent, SYN 504851 and SYN 500003*	Not Applicable

*Although the parent compound is a residue of concern in rotational crops, tolerances are not needed for the present uses, based on the absence of residues in the field rotational crops study following the label's 30 day plantback interval.

There are no data available depicting residues of mandipropamid in fresh or dried basil. As a surrogate, ARIA had translated data from vegetables, leafy (Crop Group 4) (Table 5.1.2). These data support the recommended tolerance of 20 ppm in/on fresh basil. A conservative tolerance of 240 ppm in/on basil, dried is recommended to accommodate a maximum theoretical concentration factor of 12X.

Table 5.1.2. Summary of Residue Chemistry Considerations

Parameter	Proposed Use on Basil	Translated Residue Data from Leafy Vegetables
Chemical	Mandipropamid	Mandipropamid
Formulation	Revus™	Revus™
Crop	Basil	Leafy vegetable
Type of Application	Ground, Aerial, Chemigation	Ground, Aerial, Chemigation
Number of Applications	4	4
Timing/Retreatment Interval	Post emergent foliar spray	Post emergent foliar spray
Individual Application Rate	0.13 lb ai/A	0.13 lb ai/A
Seasonal Application Rate	0.52 lb ai/A	0.52 lb ai/A
Pre-harvest Interval	7 day	1 day
Maximum Residue	---	12.8 ppm
Restrictions	Non-ionic surfactant may be used.	Non-ionic surfactant may be used.
Residue Data Source	Section 18 09IL01	DP#328534, D. McNeilly, 08/28/2007
Performing Laboratory	Not Applicable	Field Trial Studies

There are no specific Codex, Canadian, or Mexican maximum residue limits (MRLs) for mandipropamid.

The maximum seasonal application proposed for the Section 18 use on basil is less than or equal to currently registered use rates. As such, a previously modeled Tier I drinking water assessment

Mandipropamid Risk Assessment Document DP Num: 374096
 conducted by EFED for the established mandipropamid uses(DP Num: 339258, I. Abdel-Saheb, 23/APR/2007) was used in this assessment. The assessment included mandipropamid and its major aquatic degradates (SYN 500003 and SYN 5044851) in drinking water. The estimated drinking water concentrations (EDWCs) are based on the highest labeled use pattern of 4 applications of 0.13 lbs ai/A for a total rate of 0.52 lbs ai/A/Season. The modeled EDWCs are shown in the Table 5.1.3. The EDWC used in the dietary analysis is 36.5 ppb, the sum of the surface water numbers for Mandipropamid, SYN500003, and SYN504851.

	Mandipropamid (ppb)	SYN500003 (ppb)	SYN504851 (ppb)	
Surface Water	25.2	2.32	8.99	Four applications at 0.13 lb ai/A with 7 days between applications
Ground Water	5.22E-02	5.85E-01	1.73	

Note: The chronic drinking water values were incorporated directly into the dietary assessments under the DEEM-FCID food categories "water, all sources" and "water, indirect, all sources."

5.2 Dietary Exposure and Risk

A chronic dietary risk assessment was conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™, Version 2.03) which uses food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998.

No acute dietary endpoint could be identified based on the toxicology data currently available for mandipropamid and mandipropamid is classified as not likely to be a human carcinogen. Therefore, acute and cancer risks are not of concern.

A tolerance level (unrefined) chronic exposure assessment that assumes 100% crop treated was conducted for the registered and proposed Section 18 uses of mandipropamid. The DEEM analysis incorporates estimates of drinking water concentrations from EFED directly into the analysis. The chronic dietary exposure analysis for mandipropamid results in dietary risk estimates for food and water that are below the Agency's level of concern for chronic dietary exposure. For mandipropamid, the DEEM chronic dietary exposure estimate was 26% of the cPAD for the U.S. population and was 44% of the cPAD for the highest exposed population subgroup, children 1-2 years of age.

Population Subgroup	Chronic Dietary		Cancer	
	Dietary Exposure (mg/kg/day)	% cPAD	Dietary Exposure (mg/kg/day)	Risk
General U.S. Population	0.012927	26	N/A	N/A
All Infants (< 1 year old)	0.009489	19		
Children 1-2 years old	0.022136	44 ¹		
Children 3-5 years old	0.019329	39		
Children 6-12 years old	0.013175	26		
Youth 13-19 years old	0.010474	21		

Mandipropamid

Risk Assessment Document

DP Num: 374096

Population Subgroup	Chronic Dietary		Cancer	
	Dietary Exposure (mg/kg/day)	% cPAD	Dietary Exposure (mg/kg/day)	Risk
Adults 20-49 years old	0.012470	25		
Adults 50+ years old	0.012470	25		
Females 13-49 years old	0.012212	24		

¹The population subgroup with the highest estimated chronic dietary (food + drinking water) exposure and risk is indicated by bold text.

Note: % cPAD reported to 2 significant figures.

6.0 Residential and Other Exposures (Spray Drift, etc.)

Residential exposures were not assessed because the registered and proposed uses of mandipropamid do not involve applications by homeowners or by commercial applicators in residential settings.

Based on the available toxicity database and the Agency's current practices, a quantitative postapplication inhalation exposure assessment was not performed for mandipropamid at this time primarily because it has a low vapor pressure ($<7.0 \times 10^{-9}$ mmHg) and it is applied at a relatively low rate. However, volatilization of pesticides may be a potential source of postapplication inhalation exposure to individuals nearby to pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009. The Agency received the SAP's final report on March 2, 2010 (<http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html>). The Agency is in the process of evaluating the SAP report and may, as appropriate, develop policies and procedures to identify the need for and, subsequently, the way to incorporate postapplication inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative postapplication inhalation exposure assessment for mandipropamid.

Spray drift is always a potential source of exposure to residents near spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for mandipropamid. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. On a chemical by chemical basis, the Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new database submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift with specific products with significant risks associated with drift.

Mandipropamid

Risk Assessment Document

DP Num: 374096

7.0 Aggregate Risk Assessments and Risk Characterization

In accordance with the FQPA, ARIA 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, ARIA considers both the route and duration of exposure.

There are no residential uses proposed or registered for mandipropamid, and therefore aggregate risk is equal to that from consumption of food and water. Chronic aggregate risk estimates associated with exposure to mandipropamid residues in food and water do not exceed ARIA's level of concern. See section 5.2 for additional details. Acute and cancer aggregate risks are not of concern due to the absence of an acute dietary endpoint and because mandipropamid is not likely to be carcinogenic.

8.0 Cumulative Risk Characterization/Assessment

Section 408(b)(2)(D)(v) of the FFDCFA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information concerning the cumulative effects" of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to mandipropamid and any other substances, and mandipropamid does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that mandipropamid has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at <http://www.epa.gov/pesticides/cumulative/>.

9.0 Occupational Exposure/Risk Pathway

Exposure to pesticide handlers is likely during the use of mandipropamid in a variety of occupational environments. The product may be applied using groundboom equipment, aerial equipment, chemigation, and airblast equipment (grapes only).

The quantitative exposure/risk assessment developed for occupational handlers is based on the following scenarios: (1) mixing/loading liquids for aerial applications; (2) mixing/loading liquids for chemigation applications; (3) mixing/loading liquids for groundboom applications; (4) mixing/loading liquids for airblast applications; (5) applying sprays with aerial equipment; (6) applying sprays with groundboom equipment; (7) applying sprays with airblast equipment; and (8) flagging for aerial spray applications. Occupational exposures are expected to be short- and

Mandipropamid

Risk Assessment Document

DP Num: 374096

intermediate-term. ARIA does not expect long-term exposure due to the limited number of applications.

9.1 Short-/Intermediate-Term Occupational Handler Risk

Short- and intermediate-term dermal exposures and risks were not assessed for mandipropamid, since no short- or intermediate-term dermal endpoint was identified. Short-term and intermediate-term inhalation risk assessments were completed based on the inhalation toxicity endpoint that was identified. Long-term handler exposures are not expected to occur based on the uses of mandipropamid.

Daily Exposure: Daily inhalation handler exposures are estimated for each applicable handler task with the application rate, the area treated in a day, and the applicable inhalation unit exposure. The daily inhalation dose is calculated by normalizing the daily inhalation exposure by body weight and adjusting with an appropriate inhalation absorption factor.

Daily Dose: The daily inhalation dose is calculated by normalizing the daily inhalation exposure by body weight and adjusting with an appropriate inhalation absorption factor.

Margins of Exposure: Non-cancer inhalation risks for each applicable handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the daily dose to the relevant toxicological points of departure.

All short- and intermediate-term inhalation risk estimates meet or exceed the MOE of 100 at the baseline level of mitigation. This indicates that occupational inhalation risks are not of concern. A summary of the short- and intermediate-term inhalation risk estimates for each exposure scenario is presented below in Table 9.1.

Table 9.1. Summary of Exposure & Risk to Occupational Handlers From Mandipropamid.						
Unit Exposure ¹ mg ai/lb handled		Applic. Rate ² lb ai/unit	Units Treated ³	Avg. Daily Exposure ⁴ mg ai/kg bw/day		MOE ⁵
<i>Mixer/Loader - Liquid - Open Pour</i>						
Inhalation	0.0012	0.13 lb ai/A	350 A/day	Inhalation	0.00078	53,000
<i>Applicator - Air-blast - Open Cab</i>						
Inhalation	0.0045	0.13 lb ai/A	40 A/day	Inhalation	0.00033	124,000
<i>Aerial Applicator (Pilots not required to wear gloves)</i>						
Inhalation	0.000068	0.13 lb ai/A	350 A/day	Inhal.	0.000044	932,000

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing **No Gloves**; Single Layer Work Clothing **With Gloves**; Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.

2. Applic. Rate. = Taken from draft supplemental label.

3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; ExpoSAC SOP No. 9.1. Revised 5 July 2000.

4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated ÷ 70 kg Body Weight.

5. MOE = Margin of Exposure = NOAEL ÷ ADD. NOAEL for short- and intermediate-term duration inhalation exposure = 41 mg ai/kg bw/day.

9.2 Short-/Intermediate-Term Occupational Post-application Risk

Mandipropamid

Risk Assessment Document

DP Num: 374096

Occupational post-application exposures/risks were not quantified because no appropriate dermal endpoints were identified. The 4-hr Restricted Entry Interval (REI) appearing on the product label for Revus™ Fungicide adequately supports the Worker Protection Standard (WPS).

Based on the Agency's current practices, a quantitative post-application inhalation exposure assessment was not performed for mandipropamid at this time primarily because it has a very low vapor pressure ($<7.0 \times 10^{-9}$ mmHg) and is applied at a very low rate. However, volatilization of pesticides may be a potential source of post-application inhalation exposure to individuals nearby to pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009. The Agency received the SAP's final report on March 2, 2010 (<http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html>). The Agency is in the process of evaluating the SAP report and may, as appropriate, develop policies and procedures to identify the need for and, subsequently, the way to incorporate post-application inhalation exposure into the Agency's risk assessments. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative post-application inhalation exposure assessment for mandipropamid.

10.0 References:

MANDIPROPAMID – Human Occupational Exposure/Risk Assessment for the Illinois Section 18 Use of Mandipropamid on Basil, DP Num: 371728, M. Dow, 29/DEC/2009.

MANDIPROPAMID – Exposure/Risk Assessment for the Proposed Uses of Mandipropamid on *Brassica* Vegetables, Bulb Vegetables, Cucurbits, Fruiting Vegetables, Leafy Green Vegetables, Grapes, Tomatoes, and Tuberous and Corn Vegetables, DP Num: 357873, M. Dow, 28/OCT/2008.

Mandipropamid. Section 3 Registration Request to Register New Uses on Hops and Tobacco. Summary of Analytical Chemistry and Residue Data. DP Num: 348229 and 352322, Debra Rate, 11/DEC/2008.

Mandipropamid. Request to Register New Food/Feed Uses on Head and Stem *Brassica*, Leafy *Brassica* Greens, Cucurbit Vegetables, Fruiting Vegetables, Leafy Vegetables, Tuberous and Corn Vegetables, Grapes, and Onions (Dry Bulb and Green). Summary of Analytical Chemistry and Residue Data. Petition Numbers 6F7057 and 7F7184. DP Num: 340784, Dennis McNeilly, 28/AUG/2007.

Mandipropamid: Chronic Dietary (Food and Drinking Water) Exposure and Risk Assessment for Section 18 use of Mandipropamid to Basil. PC Code: 036602. DP Num: 371321. R. Chesser. 12/JAN/2010.

Mandipropamid: AMENDED Chronic Dietary (Food and Drinking Water) Exposure and Risk Assessment for Section 18 use of Mandipropamid to Basil. PC Code: 036602. DP Num: 376967. R. Chesser. 27/APR/2010.

Mandipropamid

Risk Assessment Document

DP Num: 374096

Appendix A: Tolerance Setting

Table A.1. Tolerance Summary for Mandipropamid.			
Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; <i>Correct Commodity Definition</i>
Proposed Time-limited Tolerances			
Basil, fresh	---	20	Recommended tolerance translated from vegetables, leafy (Crop Group 4).
Basil, dried	---	240	Recommended tolerance for basil, fresh, multiplied by a maximum theoretical concentration factor of 12X.

Appendix B: Review of Human Research

The PHED Task Force, 1995. The Pesticide Handlers Exposure Database, Version 1.1. Task Force members Health Canada, U.S. Environmental Protection Agency, and the National Agricultural Chemicals Association, released February, 1995.



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