United States
Environmental Protection
Agency

Prevention, Pesticides
and Toxic Substances
(7508C)

EPA 738-R-03-002
May 29, 2003

Reregistration Eligibility Decision (RED)

Dinocap

Reregistration Eligibility Decision

for

Dinocap

List B
Case 2200

May 29, 2003

This document explains the U.S. Environmental Protection Agency's (hereafter referred to as EPA or "the Agency") reregistration eligibility decision (RED) for dinocap which consists of a voluntary cancellation of all products registered in the U.S. Because the registrant, Dow AgroSciences, LLC (DAS) has expressed interest in retaining existing tolerances for apples and grapes for import purposes, this document presents only a dietary risk assessment for those uses and specifically addresses the data requirements for support of the import tolerances. The following RED document provides background information on the pesticide registration, reregistration and tolerance reassessment, an overview of the uses and health effects associated with dinocap and a summary of what data are required to support the tolerances on apples and grapes imported into the U.S., in the absence of a U.S. registration.

I. Introduction

In 1988, the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) was amended to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act provides a schedule for the reregistration process. There are five phases to the reregistration process. The first four phases of the process focus on identification of data requirements to support the reregistration of an active ingredient and the generation and submission of data to fulfill the requirements. The fifth phase is a review by the of all data submitted to support reregistration.

FIFRA requires the Agency to determine whether pesticides containing an active ingredient are eligible for reregistration before calling in data on products and either reregistering products or taking other appropriate regulatory action. Thus, reregistration involves a thorough review of the scientific data base underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether or not the pesticide meets the "no unreasonable adverse effects" criteria of FIFRA.

On August 3, 1996, the Food Quality Protection Act of 1996 (FQPA) was signed into law. This Act amends FIFRA to require that by 2006 EPA must review all tolerances in effect at the time of enactment. FQPA also amends the Federal Food, Drug and Cosmetic Act (FFDCA) to require a safety finding in tolerance reassessment based on factors including an assessment of cumulative effects of chemicals with a common mechanism of toxicity. At this time, the Agency does not have sufficient reliable information concerning common mechanism to determine whether or not dinocap shares a common mechanism of toxicity with other chemicals. Therefore, for the purpose of this risk assessment, the Agency has assumed that dinocap does not share a common mechanism with any other chemical.

II. Regulatory Background

Dinocap was the subject of a Special Review because of Agency concerns about developmental toxicity. The Position Document (PD) 1 was published on January 9, 1985 (50 FR 1119) and the PD 2/3 on October 29, 1986 (51 FR 39577). Special Review was concluded with the publication of the PD 4 on February 6, 1989 (54 FR 5908). In the PD 4, the Agency required that all dinocap labels be revised to include appropriate health hazard statements and to require the use of additional protective clothing and equipment for mixer/loaders and applicators.

Dinocap, a List B chemical, was the subject of a Phase 4 Review dated January 30, 1991 and a Data-Call-In Notice (DCI) issued on September 10, 1991. At that time, the current registrant Rohm and Haas Company (R&H) had indicated that they intended to amend registrations to drop all food/feed uses for end-use products (EPs). In the Phase 4 Review, data were required under residue chemistry guidelines pending submission of the required amendment forms and revised labels for all EPs confirming that food/feed uses had been removed. In their 90-day response to the Phase 4 DCI, R&H requested a waiver of residue chemistry data requirements based on their intention to delete all food/feed uses from their product labels. The registrant subsequently requested that the Agency retain dinocap tolerances for apples and grapes as import tolerances. Following cancellation by R&H of all dinocap food/feed uses registered in the U.S., the Agency revoked all dinocap tolerances, except those for apples and grapes (63 FR 206, October 26, 1998).

The registration for dinocap was transferred from R&H to DAS on September 21, 2001. On February 12, 2002, DAS requested voluntary cancellation pursuant to Section 6(f) of FIFRA of their U.S. product registrations for dinocap for the products Karathane WD Ag Fungicide and Miticide (EPA Registration No. 62719-384), Karathane Liquid Concentrate Ag Fungicide and Miticide (EPA Registration No. 62719-385) and Karathane Technical Ag Fungicide and Miticide (EPA Registration No. 62719-390). The Agency announced its receipt of the above-mentioned cancellation requests in the Federal Register on April 26, 2002 [OPP-2002-0013; FRL-6833-8]. The Agency did not receive any comments specific to these cancellations; therefore, the cancellation order was effective on October 24, 2002. Because dinocap products have not been marketed in the U.S. for several years, existing stocks are expected to be negligible.

III. Uses

Dinocap is a foliar fungicide/miticide used to control powdery mildew. Dinocap is applied to apples and grapes outside of the U.S., mainly in Europe, the Middle East and northern Africa. There are currently no registered dinocap products in the U.S. DAS, the registrant of dinocap, intends to support tolerances for dinocap residues in/on apples and grapes to permit legal importation of these commodities into the U.S.

IV. Health Effects

The doses and endpoints for dietary risk assessment were selected by the Hazard Identification Assessment Review Committee (HIARC) (memo dated February 23, 2000). The

HIARC established an acute toxicity endpoint for females of reproductive age (females 13+ years old) and determined that a risk assessment for acute dietary exposure is not necessary for the general population. The acute endpoint was derived from a mouse developmental study (MRID 41313001) based on a slight (nonsignificant) increase in incidences of cleft palate and eyelids-open relative to controls that occurred in the absence of maternal toxicity. The No Observed Adverse Effect Level (NOAEL) was 4 mg/kg/day and the Lowest Observed Adverse Effect Level (LOAEL) was 10 mg/kg/day.

The chronic dietary endpoint was selected from a chronic feeding study in dogs (MRID 41065401, Acc. Nos. 247957 & 247959). The NOAEL for systemic toxicity was 0.375 mg/kg/day and the LOAEL was 1.5 mg/kg/day based on effects on the eye.

The FQPA committee recommended that the FQPA safety factor for the protection of infants and children be retained at 10x for all population subgroups when assessing acute and chronic exposure. The reasons are: (1) there is concern for the quantitative and qualitative increase in susceptibility observed in fetuses following *in utero* exposure in the prenatal developmental studies in mice and rabbits; and (2) there is a data gap for the developmental neurotoxicity study in the rat.

The acute reference dose (aRfD) is 0.04 mg/kg/day and the acute population adjusted dose (aPAD) is 0.004 mg/kg/day. The chronic reference dose (cRfD) is 0.0038 mg/kg/day and the chronic population adjusted dose (cPAD) is 0.00038 mg/kg/day. The population adjusted dose is the reference dose divided by the FQPA safety factor.

The Agency has classified dinocap as a Group E "not likely" carcinogen. It was negative for inducing mutations in all studies of the standard mutagenicity battery except the Ames test. In Ames studies, dinocap was weakly positive at best and only at high doses.

For more detailed information on the potential health effects associated with dinocap, please refer to the "Dinocap Toxicology Chapter for the RED," dated April 18, 2000, which is available on the Agency's web page at *http://www.cfpub.epa.gov/oppref/rereg/status.cfm?show=rereg* and in the Public Docket.

V. Dietary Risk Assessment

Acute and chronic dietary exposure assessments were conducted to determine the dietary exposure estimates associated with the use of dinocap in/on apples and grapes to support the RED. The qualitative nature of the residue in plants and animals are not adequately understood and no acceptable magnitude of the residue or processing data in/on imported apples or grapes are currently available. Therefore, the dietary risk assessment was conducted two ways, using the current tolerances of 0.1 ppm and using Maximum Residue Limits (MRLs) recommended by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR). There are European data which have been reviewed by the JMPR. The JMPR proposes MRLs for individual pesticides in different food and feed items, and provides advice on the acceptable levels of pesticide residues in food moving in international trade. Residues of dinocap in the European trials were <0.05 (ND) to 0.09 ppm in

apples and <0.05 to 0.67 ppm in grapes. In 1988, JMPR recommended MRLs of 0.2 for apples and 1 ppm for grapes.

No processing data are available; therefore, default processing factors were used. Information is available to estimate the percent of the import apple and grape crops that are treated with dinocap. Less than 5% of the apples and grapes consumed in the U.S. are imported and less than 1% of those are treated with dinocap. Thus, the calculated percent crop treated (% CT) for dinocap is 0.05% which has been rounded up to 0.1% in the chronic dietary risk assessment.

Dinocap acute and chronic dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model (DEEM™) software Version 7.73, which incorporates consumption data from USDA's Continuing Survey of Food Intake by Individuals (CSFII), 1989-1992. The 1989-1992 data are based on the reported consumption of more than 10,000 individuals over 3 consecutive days and therefore represent more than 30,000 unique "person days" of data.

Irrespective of the residue data used (i.e., current U.S. tolerances or MRLs), acute and chronic dietary risk estimates are well below the Agency's level of concern for all supported dinocap food uses. Acute dietary risk is <1% of the aPAD for the only subpopulation of concern, females, 13-50 years old. Chronic dietary risk is <1% of the cPAD for the U.S. general population and all subpopulations.

For more detailed information on the dietary risk assessment for dinocap, please refer to the "Dinocap Acute and Chronic Dietary Exposure Assessment," dated November 7, 2001, which is available on the Agency's web page at *http://www.cfpub.epa.gov/oppref/rereg/status.cfm?show=rereg* and in the Public Docket.

VI. Tolerance Reassessment Summary

There are currently no registered food/feed uses of dinocap in the U.S. The established dinocap tolerances for food and feed commodities have been revoked except those for apples and grapes. DAS, the basic producer, intends to support tolerances for dinocap residues in/on apples and grapes to permit legal importation of these commodities into the U.S., in the absence of a U.S. registration.

Tolerances for dinocap are currently expressed in terms of combined negligible residues of a fungicide and insecticide that is a mixture of 2,4-dinitro-6-octylphenyl crotonate and 2,6-dinitro-4-octylphenyl crotonate in/on apples and grapes at 0.1 ppm [40 CFR §180.341(a)]. Current U.S. tolerances are 0.1 ppm (negligible) on both crops [40 CFR §180.341].

There are currently no Codex MRLs established for residues of dinocap. However, in 1988, JMPR recommended dinocap MRLs of 0.2 for apples and 1 ppm for grapes. Harmonization of the tolerance expression/definition and tolerances between Codex MRLs and U.S. tolerances cannot be achieved until the outstanding metabolism and residue data have been submitted.

Table 1. Tolerance Reassessment Summary for Dinocap.

Commodity	Current Tolerance (ppm)	Reassessed Tolerance (ppm)	Comments *[Corrected Commodity Definition]*
Tolerances Established Under 40 CFR §180.341(a)			
Apples	0.1(N)[1]	To be determined[2]	*[Apple]*
Grapes	0.1(N)	To be determined	*[Grape]*

VII. Data Gaps

The toxicology database for dinocap is considered adequate for the current risk assessment. Acute, subchronic and a developmental neurotoxicity study in rats are required based on concerns for the severe effects (malformations) seen in the developmental toxicity studies in mice and rabbits, as well as for the neurological effects demonstrated in mice and dogs.

There are several data gaps for residue chemistry. Data are required to describe the qualitative nature of dinocap residues in plants and animals. Magnitude of the residue in/on imported apples and grapes must be addressed with field residue data reflecting the maximum use patterns for the representative formulations in the areas/countries where dinocap will be sold and used. DAS may not need to conduct all new studies to fulfill these requirements, but may be able to rely on existing studies developed for a foreign registration or Codex MRLs to support the proposed tolerance.

Table 2 below lists the confirmatory data requirements for supporting the apple and grape tolerances for import purposes. These requirements are consistent with EPA's "Guidance on Pesticide Import Tolerances and Residue Data for Imported Food," 65 FR 106; 35069-350-90, June 1, 2000.

Table 2. Data Requirements for Dinocap Import Tolerances.

Data Requirements	New OPPTS Guideline Number	Old Guideline Number
TOXICOLOGY		
Acute Neurotoxicity Screening Battery, Rat	870.6200	81-8
Subchronic Neurotoxicity Study, Rat		82-7
Developmental Neurotoxicity Study, Rat	870.6300	83-6
RESIDUE CHEMISTRY		
Directions for Use	860.1200	171-3

[1] (N) = negligible residues; however, the Agency is removing the "(N)" designation from all entries to conform to current Agency administrative practice.

[2] These commodities were included in the dietary risk assessment for dinocap using the *Current Tolerance* level. Additional confirmatory field trial residue data are required; therefore, the final tolerance may be revised.

Data Requirements	New OPPTS Guideline Number	Old Guideline Number
Nature of the Residue, Plants	870.1300	171-4A
Nature of the Residue, Livestock		171-4B
Storage Stability, Plants	860.1380	171-4E
Crop Field Trials (Apple & Grapes)	860.1500	171-4K
Processed Food (Apple & Grapes)	860.1520	171-4L

A ruminant metabolism study is included in the above list because wet apple pomace is a livestock feed item. In order to waive this study, registrants must convincingly document that it is unlikely that imported apples or wet pomace would be significant feed items in the U.S. or exporting countries and/or that there are not significant imports of livestock commodities.

Before conducting any toxicology or residue chemistry study, the registrant should submit study protocols for EPA comment if they have any questions regarding study design and conduct. The Agency will attempt to harmonize with international standards to the extent possible.

VIII. Regulatory Conclusion

The Agency has completed its reregistration eligibility decision for the fungicide/miticide, dinocap, which consists of a voluntary cancellation of all U.S. product registrations. Because the registrant has indicated their intention to retain the existing tolerances for apples and grapes for import purposes, EPA has conducted a dietary risk assessment for dinocap. Although there are data gaps, the Agency has used protective assumptions including a 10x safety factor and tolerance level residue values to determine that dietary risk is minimal, less than 1% of the acute and chronic PADs for all population subgroups. EPA finds that there is a reasonable certainty that no harm will result from dinocap use on apples and grapes imported into the U.S. Confirmatory data are required as outlined in the previous section.

/ s /

_____

Lois A. Rossi, Director
Special Review and Reregistration Division

Appendix B. Data Supporting Guideline Requirements for the Establishment of Import Tolerances for Dinocap

GUIDE TO APPENDIX B

Appendix B contains a listing of data requirements which support the reregistration for active ingredients within the chemical case covered by this RED. It contains generic data requirements that apply in all products, including data requirements for which a "typical formulation" is the test substance.

The data table is organized in the following formats:

1. Data Requirement (Columns 1, 2 & 3). The data requirements are listed in the order of New Guideline Number and appear in 40 CFR §158. The reference numbers accompanying each test refer to the test protocols set in the Pesticide Assessment Guidance, which are available from the National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161-0002, (703) 487-4650.

2. Use Pattern (Column 4). This column indicates the use patterns for which the data requirements apply. The following letter designations are used for the given use patterns.

   A. Terrestrial food
   B. Terrestrial feed
   C. Terrestrial nonfood
   D. Aquatic food
   E. Aquatic nonfood outdoor
   F. Aquatic nonfood industrial
   G. Aquatic nonfood residential
   H. Greenhouse food
   I. Greenhouse nonfood
   J. Forestry
   K. Residential
   L. Indoor food
   M. Indoor nonfood
   N. Indoor medical
   O. Indoor residential

3. Bibliographical Citation (Column 5). If the Agency has acceptable data in its files, this column lists the identification number of each study. Normally, this is the Master Record Identification (MRID) Number, but may be a "GS" number if no MRID number has been assigned. Refer to the Bibliography (Appendix D) for a complete citation of the study.

Appendix B. Data Supporting Guideline Requirements for the Establishment of Import Tolerances for Dinocap

New Guideline Number	Old Guideline Number	Requirement	Use Pattern	Bibliographical Citation(s)
TOXICOLOGY				
870.1100	81-1	Acute Oral Toxicity, Rat		42124301
870.6200	81-8	Acute Neurotoxicity Screening Battery, Rat		Data Gap
870.3100 870.3150	82-1A 82-1B	90-Day Subchronic Feeding, Rodent and Nonrodent (Dog)		41065401, Acc. Nos. 247957, 247959
870.6200	82-7	Subchronic Neurotoxicity Study, Rat		Data Gap
870.4100	83-1A 83-1B	Chronic Feeding Toxicity, Rodent and Nonrodent (Dog)		41065401, 44932601, Acc. Nos. 247957, 247959
870.4200	83-2A 83-2B	Chronic Carcinogenicity (Feeding), Rat and Mouse		41065401, Acc. No. 247959
870.3700	83-3A 83-3B	Prenatal Developmental Toxicity, Rodent and Rabbit		40315401, 41313001, Acc. Nos. 251713, 252443, 255892, 256934, 259645
870.3800	83-4	2-Generation Reproduction and Fertility Effects, Rat		41542501, Acc. No. 254950
870.4300	83-5	Combined Chronic Toxicity/ Carcinogenicity Study, Rat		41065401, Acc. No. 247959
870.6300	83-6	Developmental Neurotoxicity Study, Rat		Data Gap
870.5140	84-2A	Gene Mutation (Ames Test)		46002023, 47005237, Acc. Nos. 00154778, 00256483, 00264191
870.5375	84-2B	Structural Chromosomal Aberration		Acc. Nos. 00256483, 00264191
870.5300	84-2	Detection of Gene Mutations in Somatic Cells in Culture, Mammalian		47025237, Acc. No. 00264191
870.5500	84-4	Other Genotoxic Effects		00256483
870.7600	85-2	Dermal Absorption (Penetration), Rat		Acc. Nos. 259639, 260614
RESIDUE CHEMISTRY				
860.1200	171-3	Directions for Use		Data Gap
860.1300	171-4A 171-4B	Nature of the Residue, Plants and Animals		Data Gap
860.1340	171-4C 171-4D	Residue Analytical Method, Plants and Animals		Reserved
860.1360	171-4M	Multiresidue Methods		Reserved
860.1380	171-4E	Storage Stability, Plants		Data Gap
		Storage Stability, Animals		Reserved
860.1480	171-4J	Magnitude of Residues in Meat, Milk, Poultry and Eggs		Reserved

New Guideline Number	Old Guideline Number	Requirement	Use Pattern	Bibliographical Citation(s)
Miscellaneous Commodities Group				
860.1500	171-4K	Crop Field Trials (Grapes)		Data Gap
Pome Fruits Group				
860.1500	171-4K	Crop Field Trials (Apple)		Data Gap
Processed Food/Feed Group				
860.1520	171-4L	Processed Food (Apple)		Data Gap
		Processed Food (Grapes)		Data Gap