United States Environmental Protection Agency

Office of Prevention, Pesticides and Toxic Substances (7505P)

Pesticide Fact Sheet

Name of Chemical: **Meptyldinocap**
Reason for Issuance: **New Chemical**
Tolerance Established
Date Issued: **September 2009**

Description of Chemical

Generic Name:	2-(1-methylheptyl)-4,6-dinitrophenyl (2*E*)-2-butenoate
Common Name:	Meptyldinocap
Trade Name Used: In Foreign Countries:	GF-1478 Fungicide
Chemical Class:	Dinitrophenol
EPA Chemical Code:	036000
Chemical Abstracts Service (CAS) Number:	131-72-6
Registration Status:	Not Registered in the U.S.; Import Tolerance Established
Pesticide Type:	Fungicide
U.S. Producer:	Dow AgroSciences, LLC 9330 Zionsville Road Indianapolis, IN 46268

Tolerances Established

An import tolerance for the combined residues of meptyldinocap (2-(1-methylheptyl)-4,6-dinitrophenyl (2*E*)-2-butenoate) and 2,4-DNOP (2,4-dinitro-6-(1-methylheptyl)phenol) expressed as meptyldinocap for use on grapes at 0.2 ppm was established in the 40 CFR §180.648.

Use Patterns and Formulation

Meptyldinocap is a new dinitrophenol fungicide and is one of six isomers found in the older fungicide dinocap. Meptyldinocap is used on grapevines in the United Kingdom, Italy, Romania, Hungary, Tunisia, and Chile to control powdery mildew. Meptyldinocap is proposed for use in these countries as a 350 g/L emulsifiable concentrate (EC) formulation labeled for multiple foliar applications per season. Meptyldinocap interferes with fungal respiration by acting as an uncoupler of oxidative phosphorylation, and has been placed in Group 29 by the Fungicide Resistance Action Committee (FRAC). There are currently no meptyldinocap products registered in the U.S. A summary of the use pattern in foreign countries is provided in Table 1 below.

Table 1 Maximum Application Rate of Meptyldinocap on Grapes in Several European Countries and Tunisia

App. Timing, Type, and Equip.	Formulation	App. Rate (kg ai/ha)	Max. No. App. per Season	Max. Seasonal App. Rate (kg ai/ha)	PHI (days)	Use Directions and Limitations
Broadcast foliar - BBCH growth stage 13 to 81(3 leaves unfolded; beginning of ripening); broadcast application by ground equipment	350 g/L EC	0.21	4	0.84	21	Retreatment interval (RTI) = 10 days, RTI of 5 days when used as an eradicant late in the season (only two applications may be made as a late season eradicant)
Maximum Application Rate of Meptyldinocap on Grapes in Chile						
Broadcast foliar - swollen-bud to preflower and postharvest; broadcast application by ground equipment	350 g/L EC	preharvest - 0.21 postharvest - 0.41	3	not indicated	60	RTI = 7 days.

Product Chemistry

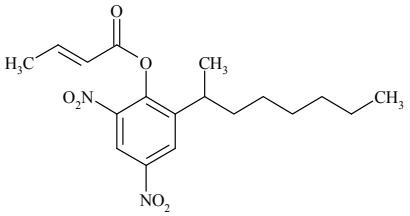
Table 2 Nomenclature of Meptyldinocap	
Structure	
Common name	Meptyldinocap (also referred to as 2,4-dinitro-6-(1-methylheptyl) crotonate)
Company experimental name	DE-126; RH-23,163
IUPAC name	(*RS*)-2-(1-methylheptyl)-4,6-dinitrophenyl crotonate
CAS name	2-(1-methylheptyl)-4,6-dinitrophenyl (2*E*)-2-butenoate
CAS registry number	131-72-6
Molecular weight	364.40
End-use product (EP)	350 g/L EC (GF-1478 Fungicide; 33.2% EC)

Table 3 Physicochemical Properties	
Melting point	-22.5°C
pH	not applicable
Relative density	1.11
Water solubility (mg/L) at 20°C	0.151
Solvent solubility (g/L) at 25°C	Acetone >252 Ethyl acetate >256 1,2-Dichloroethane >252 Xylene >256 n-Heptane >251 Methanol >253
Vapor pressure (Pa) at 25°C	7.92×10^{-6}
Dissociation constant, pK_a	Does not dissociate in aqueous solutions.
Octanol/water partition coefficient, $Log(K_{OW})$ at 20.5°C	6.55 ± 0.33
UV/visible absorption spectrum (maxima, molar extinction coefficient)	acidic: 240 nm (ε=16727), 310 nm (ε=2155) basic: 260 nm (ε=6376), 372 nm (ε=12980), 405 nm (ε=10969) neutral: 240 nm (ε=16727), 310 nm (ε=2155)

Toxicology Profile

Table 4 Acute Toxicity Profile – Technical Meptyldinocap				
Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral (rat)	47289116	LD_{50} > 2000 mg/kg bw (F)	III
870.1200	Acute dermal (rat)	47289118	LD_{50} > 5000 mg/kg bw (M&F)	IV
870.1300	Acute inhalation (rat)	N/A	N/A	N/A

870.2400	Primary eye irritation (rabbit)	47289120	Minimally irritating	III
870.2500	Primary dermal irritation (rabbit)	47289122	Slight irritant	IV
870.2600	Dermal sensitization (mouse)	47289124	Positive (LLNA)	N/A

Table 5 Subchronic, Chronic and Genotoxicity Profile for Meptyldinocap

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3050 28-Day oral toxicity (mouse)	47289127 (2005) **Acceptable/non-guideline** 0, 100, 200, or 750 ppm (equivalent to 0/0, 16/19.3, 30.7/40.8, or 117/161.1 mg/kg bw/day [M/F])	NOAEL = 750 ppm (117/161.1 mg/kg bw/day [M/F]) LOAEL not observed.
870.3100 90-Day oral toxicity (rat)	47289128 (2005) **Acceptable/guideline** 0, 200, 650, or 2000 ppm (equivalent to 0/0, 11/13, 37/41, or 113/127 mg/kg bw/day [M/F])	NOAEL = 650 ppm (37/41 mg/kg bw/day [M/F]) LOAEL = 2000 ppm (113/127 mg/kg bw/day [M/F]), based on decreased body weight, body-weight gain, and food consumption in both sexes.
870.3150 90-Day oral toxicity (dog)	47289129 (2005) **Acceptable/guideline** 0, 15, 60, or 120 ppm (equivalent to 0/0, 0.49/0.48, 1.51/2.14, or 3.58/3.89 mg/kg bw/day [M/F])	NOAEL = 60 ppm (1.51 mg/kg bw/day [M]) LOAEL = 120 ppm (3.58 mg/kg bw/day) based on significant, sustained increased alanine aminotransferase (ALT) and aspartame aminotransferase (AST) levels (M).
870.4100 1-year oral toxicity (dog) Extension of 90-day study without a control group	47289130 (2006) **Acceptable/non-guideline** 120 ppm (equivalent to 3.31/3.22 mg/kg bw/day [M/F])	No effect of treatment at 120 ppm on limited number of parameters, including ophthalmological measurements.
870.3700 Prenatal developmental (mouse)	47289132 (2005) **Acceptable/non-guideline** 0, 100, 250, or 500 mg/kg bw/day)	Maternal NOAEL = 500 mg/kg bw/day Maternal LOAEL not observed. Developmental NOAEL = 500 mg/kg bw/day Developmental LOAEL not observed. No effect on external or otoconial development.
870.3700 Prenatal developmental (rat)	47289134 (2005) **Acceptable/guideline** 0, 50, 150, [or 500	Maternal NOAEL = 50 mg/kg bw/day Maternal LOAEL = 150 mg/kg bw/day based on decreased body weights, body-weight gains, and food consumption.

Table 5 Subchronic, Chronic and Genotoxicity Profile for Meptyldinocap

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
	(terminated)] mg/kg bw/day)	Developmental NOAEL = 150 mg/kg bw/day Developmental LOAEL not observed. Developmental toxicity was not observed, including effects on otoconial development.
870.3700 Prenatal developmental (rabbit)	47289136 (2005) **Acceptable/guideline** 0, 3, 12, or 48 mg/kg bw/day	Maternal NOAEL = 12 mg/kg bw/day Maternal LOAEL = 48 mg/kg bw/day based on decreased body-weight gains and food consumption. Developmental NOAEL = 48 mg/kg bw/day Developmental LOAEL not observed. Developmental toxicity was not observed, including effects on otoconial development.
Special study Oral developmental toxicity with non-methylheptyl isomers of dinocap (mice)	47289133 (2005) **Acceptable/non-guideline** 5 or 10 mg/kg bw/day, depending on isomer	Developmental toxicity was observed with the 2,6-dinitro-4-(1-propylpentyl)-phenyl crotonate (4-PP) isomer of dinocap only.
Special study Oral developmental and postnatal toxicity with methylheptyl isomers of dinocap and dinocap (mice)	47304907 (1987) **Acceptable/non-guideline** 25 mg/kg bw/day	No evidence of developmental toxicity, incl. cleft palate or torticollis and no effects on fetal body weight, swimming ability, or otolith development with either methylheptyl isomer or in combination. Also published in Rogers et al. 1987. Teratogenesis, Carcinogenesis, and Mutagenesis 7:341-346.
870.5100 Bacterial gene mutation	47289137 (2005) **Acceptable/guideline** 0-4690 µg/plate (+/- S9)	Negative
870.5300 Mammalian cell gene mutation	47289138 (2005) **Acceptable/guideline** 0-18.6 µg/mL (-S9) 0-92.9 µg/mL (+S9)	Negative
870.5375 *In vitro* mammalian chromosomal aberration	47289139 (2005) **Acceptable/guideline** 0-929 µg/mL (+/-S9)	Negative

Table 5 Subchronic, Chronic and Genotoxicity Profile for Meptyldinocap

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.5395 *In vivo* mouse erythrocyte micronucleus assay	47289140 (2005) **Acceptable/guideline** 0, 465, 929, or 1858 mg/kg bw	Negative
870.7485 Metabolism and pharmacokinetics	47289141 (1996) **Acceptable/non-guideline** 29.5 (mice) or 95.5 (rats) mg/kg bw (single dose)	This study was performed to evaluate differences in rat and mouse urinary metabolism (only) of meptyldinocap as a surrogate for dinocap. Fatty acid β-oxidation was the primary metabolic pathway in both species; more metabolism occurred via fatty acid α-oxidation in mice (approximately 32.9%) than in the rats (18.0%). A total of 7 metabolites were identified in mouse urine that were not identified in rat urine; however, each compound represented only 1.23-2.78% of the total radioactivity isolated in the urine. Based on these results, 2,4-DNHPC undergoes esterase-mediated de-esterification followed by sequential metabolism by cytochrome P-450, alcohol dehydrogenase, and aldehyde dehydrogenase to form the carboxylated metabolite, 2,4-dinitro-6-(1-methylheptanoate)phenol. Further metabolism proceeds via the fatty acid pathways, which is the primary pathway for metabolism of 2,4-DNHPC in both rat and mouse.
870.7485 Metabolism and pharmacokinetics	00153615, 47289142 (1976) **Acceptable/non-guideline** 49 mg/kg bw/day (7 days; 1 rat/sex)	Absorption: 18-24% administered dose throughout 7 days. Distribution: largest concentrations of radioactive residues (excluding the GI tract) included heart, carcass, liver, pelt, and thymus (0.27-0.85% administered dose). Metabolism: hydrolysis of the crotonate ester followed by oxidation of the octyl side chain. Excretion: primarily through the feces (52-58% administered dose) and urine (15-20% administered dose) throughout 7 days.

Table 5 Subchronic, Chronic and Genotoxicity Profile for Meptyldinocap			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.3050	28-Day oral toxicity (mouse)	47289127 (2005) **Acceptable/non-guideline** 0, 100, 200, or 750 ppm (equivalent to 0/0, 16/19.3, 30.7/40.8, or 117/161.1 mg/kg bw/day [M/F])	NOAEL = 750 ppm (117/161.1 mg/kg bw/day [M/F]) LOAEL not observed.
870.3100	90-Day oral toxicity (rat)	47289128 (2005) **Acceptable/guideline** 0, 200, 650, or 2000 ppm (equivalent to 0/0, 11/13, 37/41, or 113/127 mg/kg bw/day [M/F])	NOAEL = 650 ppm (37/41 mg/kg bw/day [M/F]) LOAEL = 2000 ppm (113/127 mg/kg bw/day [M/F]), based on decreased body weight, body-weight gain, and food consumption in both sexes.
870.3150	90-Day oral toxicity (dog)	47289129 (2005) **Acceptable/guideline** 0, 15, 60, or 120 ppm (equivalent to 0/0, 0.49/0.48, 1.51/2.14, or 3.58/3.89 mg/kg bw/day [M/F])	NOAEL = 60 ppm (1.51 mg/kg bw/day [M]) LOAEL = 120 ppm (3.58 mg/kg bw/day) based on significant, sustained increased alanine aminotransferase (ALT) and aspartame aminotransferase (AST) levels (M).
870.4100	1-year oral toxicity (dog) Extension of 90-day study without a control group	47289130 (2006) **Acceptable/non-guideline** 120 ppm (equivalent to 3.31/3.22 mg/kg bw/day [M/F])	No effect of treatment at 120 ppm on limited number of parameters, including ophthalmological measurements.
870.3700	Prenatal developmental (mouse)	47289132 (2005) **Acceptable/non-guideline** 0, 100, 250, or 500 mg/kg bw/day)	Maternal NOAEL = 500 mg/kg bw/day Maternal LOAEL not observed. Developmental NOAEL = 500 mg/kg bw/day Developmental LOAEL not observed. No effect on external or otoconial development.
870.3700	Prenatal developmental (rat)	47289134 (2005) **Acceptable/guideline** 0, 50, 150, [or 500 (terminated)] mg/kg bw/day)	Maternal NOAEL = 50 mg/kg bw/day Maternal LOAEL = 150 mg/kg bw/day based on decreased body weights, body-weight gains, and food consumption. Developmental NOAEL = 150 mg/kg bw/day Developmental LOAEL not observed. Developmental toxicity was not observed, including effects on otoconial development.

Table 5 Subchronic, Chronic and Genotoxicity Profile for Meptyldinocap			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.3700	Prenatal developmental (rabbit)	47289136 (2005) **Acceptable/guideline** 0, 3, 12, or 48 mg/kg bw/day	Maternal NOAEL = 12 mg/kg bw/day Maternal LOAEL = 48 mg/kg bw/day based on decreased body-weight gains and food consumption. Developmental NOAEL = 48 mg/kg bw/day Developmental LOAEL not observed. Developmental toxicity was not observed, including effects on otoconial development.
Special study	Oral developmental toxicity with non-methylheptyl isomers of dinocap (mice)	47289133 (2005) **Acceptable/non-guideline** 5 or 10 mg/kg bw/day, depending on isomer	Developmental toxicity was observed with the 2,6-dinitro-4-(1-propylpentyl)-phenyl crotonate (4-PP) isomer of dinocap only.
Special study	Oral developmental and postnatal toxicity with methylheptyl isomers of dinocap and dinocap (mice)	47304907 (1987) **Acceptable/non-guideline** 25 mg/kg bw/day	No evidence of developmental toxicity, incl. cleft palate or torticollis and no effects on fetal body weight, swimming ability, or otolith development with either methylheptyl isomer or in combination. Also published in Rogers et al. 1987. Teratogenesis, Carcinogenesis, and Mutagenesis 7:341-346.

Table 5 Subchronic, Chronic and Genotoxicity Profile for Meptyldinocap			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.5100	Bacterial gene mutation	47289137 (2005) **Acceptable/guideline** 0-4690 µg/plate (+/- S9)	Negative
870.5300	Mammalian cell gene mutation	47289138 (2005) **Acceptable/guideline** 0-18.6 µg/mL (-S9) 0-92.9 µg/mL (+S9)	Negative
870.5375	*In vitro* mammalian chromosomal aberration	47289139 (2005) **Acceptable/guideline** 0-929 µg/mL (+/-S9)	Negative
870.5395	*In vivo* mouse erythrocyte micronucleus assay	47289140 (2005) **Acceptable/guideline** 0, 465, 929, or 1858 mg/kg bw	Negative
870.7485	Metabolism and pharmacokinetics	47289141 (1996) **Acceptable/non-guideline** 29.5 (mice) or 95.5 (rats) mg/kg bw (single dose)	This study was performed to evaluate differences in rat and mouse urinary metabolism (only) of meptyldinocap as a surrogate for dinocap. Fatty acid β-oxidation was the primary metabolic pathway in both species; more metabolism occurred via fatty acid α-oxidation in mice (approximately 32.9%) than in the rats (18.0%). A total of 7 metabolites were identified in mouse urine that were not identified in rat urine; however, each compound represented only 1.23-2.78% of the total radioactivity isolated in the urine. Based on these results, 2,4-DNHPC undergoes esterase-mediated de-esterification followed by sequential metabolism by cytochrome P-450, alcohol dehydrogenase, and aldehyde dehydrogenase to form the carboxylated metabolite, 2,4-dinitro-6-(1-methylheptanoate)phenol. Further metabolism proceeds via the fatty acid pathways, which is the primary pathway for metabolism of 2,4-DNHPC in both rat and mouse.

Table 5 Subchronic, Chronic and Genotoxicity Profile for Meptyldinocap			
Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.7485	Metabolism and pharmacokinetics	00153615, 47289142 (1976) **Acceptable/non-guideline** 49 mg/kg bw/day (7 days; 1 rat/sex)	Absorption: 18-24% administered dose throughout 7 days. Distribution: largest concentrations of radioactive residues (excluding the GI tract) included heart, carcass, liver, pelt, and thymus (0.27-0.85% administered dose). Metabolism: hydrolysis of the crotonate ester followed by oxidation of the octyl side chain. Excretion: primarily through the feces (52-58% administered dose) and urine (15-20% administered dose) throughout 7 days.

Toxicological Endpoints

Table 6 Meptyldinocap - Summary of Toxicological Doses and Endpoints Used in Human Health Risk Assessment				
Exposure Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Relevant Toxicological Effects
Acute Dietary (All populations)	An endpoint of concern (effect) attributable to a single dose was not identified in the database. Quantification of acute risk to all populations was not required.			
Chronic Dietary (All populations)	NOAEL = 1.51 mg/kg bw/day	UF_A = 10x; UF_H = 10x UF_{FQPA} = 3x; (includes UF_S)	cRfD = cPAD = 0.005 mg/kg bw/day	**90-day oral (dog; dietary)** LOAEL = 120 ppm (3.58 mg/kg bw/day) based on sustained increased alanine aminotransferase (ALT) and aspartame aminotransferase (AST) levels in males
Cancer	Carcinogenicity studies with meptyldinocap were not performed. Classification of dinocap: "Group E, Evidence of non-carcinogenicity in humans"			

Abbreviations:

UF = uncertainty factor
UF_A = extrapolation from animal to human (interspecies)
UF_H = potential variation in sensitivity among members of the human population (intraspecies)
UF_{FQPA} = FQPA Safety Factor
UF_S = extrapolation from subchronic to chronic exposure
NOAEL = no observed adverse effect level
LOAEL = lowest observed adverse effect level
RfD = reference dose (a = acute, c = chronic) = NOAEL ÷ (UF_A x UF_H)
PAD = population adjusted dose = RfD ÷ UF_{FQPA}.

Food Quality Protection Act Considerations:

EPA has determined that an FQPA SF of 3X is necessary to protect the safety of infants and children given that the point-of-departure for estimating chronic human risk was chosen from a subchronic study. Use of a 3X SF, in the form of an uncertainty factor for subchronic-to-chronic extrapolation, with the NOAEL of 1.5 mg/kg/ bw/day from a 90-day toxicity study in dogs yields an effective NOAEL of 0.5 mg/kg/ bw/day for meptyldinocap. EPA concludes that reliable data support this FQPA SF based upon the following considerations:

1) The adjusted NOAEL for meptyldinocap is virtually identical to the NOAEL used for the cRfD for dinocap (0.4 mg/kg bw/day). Use of a larger SF for meptyldinocap would yield a lower point of departure than that for dinocap, which would be inappropriate, given that meptyldinocap is a significantly less toxic chemical than dinocap. Evidence showing the lower toxicity of meptyldinocap include:

    - Meptyldinocap is one of six isomers contained in dinocap. Toxicological studies have isolated the teratogenic isomer in dinocap, and it is not meptyldinocap.

    - Meptyldinocap is considered less toxic than dinocap based on the lack of developmental and ocular toxicities with meptyldinocap at approximately 5X the doses contained in dinocap.

    - A comparison of subchronic studies in the mouse for dinocap with similar studies for meptyldinocap indicated that dinocap caused liver toxicity and death, whereas toxicity was absent with meptyldinocap following treatment for 28 days at a higher dose.

    - Unlike dinocap, there is no evidence of offspring susceptibility with meptyldinocap in any of four developmental toxicity studies across three species tested.

    - Unlike dinocap, there was no evidence of neurotoxicity or neuropathology in any of the submitted studies for meptyldinocap.

    - Unlike dinocap, there was no effect of treatment on mortality, clinical signs, ophthalmological examinations, or select gross or microscopic pathology in dogs treated for one year with meptyldinocap. The dinocap cRfD was based on a chronic study in dogs.

2) Evidence from the meptyldinocap dog study indicates that extending exposure from subchronic to chronic would not have produced a lower NOAEL. As indicated above, the extension of the meptyldinocap dog study for an additional 9 months did not result in effects on mortality, clinical signs, ophthalmological examinations, or select gross or microscopic pathology as it did with dinocap. Moreover, while levels of serum hepatic enzymes in dogs in the meptyldinocap study were increased significantly over controls throughout the 90-day exposure period, the serum hepatic enzyme levels did not become more severe over time.

Although EPA does not have toxicology studies conducted with meptyldinocap to fulfill all data requirements, EPA concludes that between the dinocap and meptyldinocap studies it has a complete database. The dinocap database was incomplete due to a lack of a developmental neurotoxicity study but such a study is not needed for meptyldinocap because there was no evidence of neurotoxicity or neuropathology in any of the submitted studies for meptyldinocap. These results contrast with those of dinocap in which minor neuropathology was noted in dogs treated with dinocap as a positive control for 90 days.

EPA began requiring acute and subchronic neurotoxicity testing of all food and non-food use pesticides on December 26, 2007. Since this requirement went into effect after the tolerance petition was submitted, these studies are not yet available for meptyldinocap. In the absence of specific neurotoxicity studies, EPA has evaluated the available toxicity data to determine whether an additional database uncertainty factor is needed to account for potential neurotoxicity. Given the lack of neurotoxicity or neuropathology in any meptyldinocap studies, EPA does not believe that conducting acute or subchronic neurotoxicity testing will result in a NOAEL less than 1.5 mg/kg/day already established for the cRfD for meptyldinocap, and an additional uncertainty factor is not needed to account for the lack of these data. Immunotoxicity testing is also required as a result of changes made to the pesticide data requirements in December of 2007.

An immunotoxicity study has not been conducted with meptyldinocap. However, an in vivo immunotoxicity study with additional in vitro measurements (Smialowicz, et al., 1992) has been conducted with dinocap in mice and published in the open literature. Immune function, cellularity, organ weights, and histopathology were measured over several doses in the study. Immunotoxicity was observed at a 30-fold higher dose than the effective NOAEL used to calculate the cRfD for meptyldinocap. Because a well conducted immunotoxicity study with dinocap was performed previously, and since meptyldinocap is considered less toxic than dinocap, the requirement for an immunotoxicity study with meptyldinocap has been satisfied by the literature study with dinocap.

3) There is no evidence of offspring susceptibility with meptyldinocap in any of four developmental toxicity studies across three species tested.

4) There are no residual uncertainties identified in the exposure database for meptyldinocap. The dietary food exposure assessments were performed based on 100%CT and tolerance-level residues as well as a very conservative assumption of what meptyldinocap exposure could occur from use of dinocap. No exposure to meptyldinocap in drinking water or from residential use is expected because neither meptyldinocap nor dinocap are registered for use in the United States. The exposure assessment will not underestimate the exposure and risks posed by meptyldinocap.

Exposure Assessment:

Occupational, residential and drinking water exposures were not assessed since U.S. registration was not sought for meptyldinocap. Risk estimates were based on dietary (food only) exposure to meptyldinocap residues on grapes and exposure to meptyldinocap from the currently established tolerances for dinocap use on apples and grapes under 40 CFR 180.341. The dietary risk estimates below represent the aggregate risk.

Acute Dietary Risk: An endpoint attributable to a single exposure was not identified, and therefore, a quantitative acute dietary risk assessment was not performed. Meptyldinocap is not expected to pose an acute risk.

Chronic Dietary Risk: The chronic dietary exposure assessment (food only) assumed tolerance level residues and 100% crop-treated for all potential sources of meptyldinocap (exposure to residues of meptyldinocap on imported grapes, and exposure to meptyodinocap residues from use of dinocap on imported apples and grapes). Since 22% of technical dinocap is meptyldinocap and since the proportion of dinocap residues occupied by meptyldinocap is unknown, the chronic analysis assumed that 100% of the dinocap residues on imported apples and grapes were meptyldinocap. It is estimated that chronic dietary exposure to meptyldinocap will utilize 35% of the cPAD for children 1-2 years, the population subgroup receiving the greatest exposure, and does not exceed the Agency's level of concern.

Cancer: Based on structural similarities and the demonstrated lower toxicity of meptyldinocap as compared to dinocap, the cancer classification of Group E - Evidence of non-carcinogenicity in humans for dinocap was extended to meptyldinocap.

DATA GAPS

The petitioner, Dow AgroSciences, has agreed to provide the following additional data:

1. Grape to raisin processing data (OPPTS Guideline Number 860.1520).
2. Submission of analytical standards (meptyldinocap and 2,4-DNOP) to the EPA National Pesticide Standards Repository.

3. Acute neurotoxicity screening battery study on rats (OPPTS Guideline Number 870.6200a) and subchronic (90-Day) neurotoxicity screening battery study on rats (OPPTS Guideline Number 870.6200b).

Contact person at USEPA

Mailing address:

Mary L. Waller
Product Manager (21)
Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Fungicide Branch
1200 Pennsylvania Avenue NW
Washington, D.C. 20460

Office location and telephone number:

Room S-7319, One Potomac Yard
2777 South Crystal Drive (South Tower)
Arlington, Virginia 22202

Disclaimer: The information in this Pesticide Fact Sheet is a summary only and is not to be used to satisfy any data requirements for pesticide registration or reregistration.

APPENDIX I:

GLOSSARY OF TERMS AND ABBREVIATIONS

ADNT	Acute delayed neurotoxicity
a.i.	Active Ingredient
ALT	Alanine Aminotransferase
aPAD	Acute Population Adjusted Dose
ARI	Aggregate Risk Index
AST	Aspartame Aminostransferase
BCF	Bioconcentration Factor
CAS	Chemical Abstracts Service
ChE	Cholinesterase
ChEI	Cholinesterase inhibition
cPAD	Chronic Population Adjusted Dose
%CT	Percent crop treated
DAT	Days after treatment
DEEM-FCID	Dietary Exposure Evaluation Model - Food Consumption Intake Database
DNA	Deoxyribonucleic acid
DNT	Developmental neurotoxicity
DIT	Developmental immunotoxicity
DWLOC	Drinking Water Level of Comparison.
EC	Emulsifiable Concentrate Formulation
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.

EPA	U.S. Environmental Protection Agency
FQPA	Food Quality Protection Act
GLC	Gas Liquid Chromatography
GLN	Guideline Number
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOAEL	Lowest Observed Adverse Effect Level
LOAEC	Lowest Observed Adverse Effect Concentration
LOC	Level of Concern
LOD	Limit of Detection
LOQ	Limit of quantitation
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter
MOE	Margin of Exposure
MRID	Master Record Identification (number), EPA's system of recording and tracking studies submitted
MTD	Maximum tolerated dose
NA	Not Applicable
NOEC	No Observable Effect Concentration
NOEL	No Observed Effect Level
NOAEL	No Observed Adverse Effect Level
NOAEC	No Observed Adverse Effect Concentration
NPDES	National Pollutant Discharge Elimination System
OP	Organophosphate
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
PAG	Pesticide Assessment Guideline
PAM	Pesticide Analytical Method
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/ EXAMS	Tier II Surface Water Computer Model
RAC	Raw Agriculture Commodity
RBC	Red Blood Cell
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose

SCI-GROW	Tier I Ground Water Computer Model
SF	Safety Factor
TGAI	Technical Grade Active Ingredient
UF	Uncertainty Factor
µg	micrograms
µg/L	Micrograms Per Liter
µL/g	Microliter per gram
USDA	United States Department of Agriculture
WPS	Worker Protection Standard

APPENDIX II

Citations Considered to be Part of the Data Base Supporting the Registration of Meptyldinocap.

MRID	Citation
47289100	Dow Agrosciences LLC (2007) Submission of Product Chemistry, Residue, Toxicity and Environmental Fate Data in Support of the Application for Registration of GF-1478 and the Petition for Tolerance of Meptyldinocap for Use on Apples, Wine Grapes, Cucumbers, Tomatoes, Peaches and Strawberries. Transmittal of 35 Studies
47289102	Nelson, R. (2007) Group B - Physical/Chemical Properties for GF-1478, A Liquid End Use Product Containing Meptyldinocap. Project Number: NAFST/07/134. Unpublished study prepared by Dow Agrosciences LLC. 5 p.
47289103	Byrne, S.; Thomas, A.; Hilla, S. (2003) The Nature of the Residue of (Carbon 14)-2,6-DNOPC (Dinocap) in Apples. Project Number: 020042/01. Unpublished study prepared by Dow AgroSciences LLC. 128 p.
47289104	Dohmeier, D. (1993) Nature of the Residue in Plants: Metabolism of (Carbon 14) Dinocap in Apples. Project Number: 34/93/21, 34/92/22, TR/34/92/22. Unpublished study prepared by Rohm and Haas Co. 321 p.
47289105	Dohmeier, D. (1994) Nature of the Residue in Plants: Metabolism of (Carbon 14) Dinocap in Apples: Supplement to Rohm and Haas Technical Report 34-93-21. Project Number: 34/94/14, TR/34/94/14. Unpublished study prepared by Rohm and Haas Co. 254 p.
47289106	Honeycutt, R. (1976) The Metabolism of (Carbon 14) 2,4-Dinitro-6-(2-Octyl) Phenyl Crotonate in Cucumber Fruit. Project Number: TR/3423/76/28, 3423/76/28. Unpublished study prepared by Rohm and Haas Co. 29 p.
47289107	Foster, D. (2002) Dinocap Method Validation: DNOPC and DNOP Validation of Methodology for the Determination of DNOPC and DNOP in Apples and Grapes Using LC-MS/MS. Project Number: GH/C/5503, DOS/220/DOS/220/0222962, DOS/220/022962. Unpublished study prepared by Huntingdon Life Sciences, Ltd. 74 p.
47289108	Foster, D. (2002) Dinocap Independent Laboratory Validation: DNOPC and DNOP: Independent Laboratory Validation of Methodology for the Determination of DNOPC and DNOP in Apples and Grapes Using LC-MS/MS. Project Number: DOS/221/023839. Unpublished study prepared by Huntingdon Life Sciences, Ltd. 83 p.
47289109	Howie, D.; Lees, M. (1999) Dinocap: Determination of the Storage Stability at Residue Levels of Dinocap in Cucumbers, Tomatoes, Peaches, Apples and

MRID	Citation
	Strawberries. Project Number: RAS/049, RAS/049/980207, ER/76/1/TR34/99/141. Unpublished study prepared by Huntingdon Life Sciences, Ltd. 144 p.
47289112	North, L. (2007) Residues of DE-126 in Wine Grapes at Intervals and Harvest Following Multiple Applications of GF-1478, Southern and Northern Europe - 2006. Project Number: GHE/P/11595, 10001049. Unpublished study prepared by Agrisearch UK, Ltd., DowElanco GmbH and Agrisearch France SARL. 175 p.
47289115	Jones, G. (2006) Residues of Dinocap or DE-126 in Wine Grapes at Intervals and Harvest Following Multiple Applications of GF-1344 or GF-1478, Northern Europe - 2005. Project Number: GHE/P/11344, AF/8927/DE, 10001049. Unpublished study prepared by Agrisearch UK, Ltd., DowElanco GmbH and Agrisearch France SARL. 147 p.
47289116	Merkel, D. (2005) Acute Oral Toxicity Up and Down Procedure in Rats: Dinocap II. Project Number: 17042, 050197, P320/UDP/DOW. Unpublished study prepared by Product Safety Laboratories. 28 p.
47289117	Merkel, D. (2005) Acute Oral Toxicity Up and Down Procedure in Rats: GF-1478. Project Number: 17046, 050207, P320/UDP/DOW. Unpublished study prepared by Product Safety Laboratories. 28 p.
47289118	Merkel, D. (2005) Acute Dermal Toxicity Study in Rats - Limit Test: Dinocap II. Project Number: P322/DOW, 17043, 050198. Unpublished study prepared by Product Safety Laboratories. 25 p.
47289119	Merkel, D. (2005) Acute Dermal Toxicity Study in Rats - Limit Test: GF-1478. Project Number: 17047, 050208, P322/DOW. Unpublished study prepared by Product Safety Laboratories. 27 p.
47289120	Merkel, D. (2005) Primary Eye Irritation Study in Rabbits: Dinocap II. Project Number: 17044, 050200, P324/DOW. Unpublished study prepared by Product Safety Laboratories. 27 p.
47289121	Merkel, D. (2005) Primary Eye Irritation Study in Rabbits: GF-1478. Project Number: 050210, 17048, P324/DOW. Unpublished study prepared by Product Safety Laboratories. 32 p.
47289122	Merkel, D. (2005) Primary Skin Irritation Study in Rabbits: Dinocap II. Project Number: 050199, 17045, P326/DOW. Unpublished study prepared by Product Safety Laboratories. 28 p.
47289123	Merkel, D. (2005) Primary Skin Irritation Study in Rabbits: GF-1478. Project Number: 17049, 050209, P326/DOW. Unpublished study prepared by Product Safety Laboratories. 30 p.
47289124	Woolhiser, M.; Wiescinski, C. (2005) Dinocap II (DE-126): Local Lymph Node Assay in Balb/cAnNCrl Mice. Project Number: 041156. Unpublished study prepared by Dow Chemical Co. 27 p
47289125	Woolhiser, M.; Wiescinski, C. (2005) GE-1478: Local Lymph Node Assay in Balb/cAnNCrl Mice. Project Number: 051057. Unpublished study prepared by Dow Chemical Co. 25 p.
47289127	Thomas, J.; Yano, B.; Dryzga, M. (2005) Dinocap II (DE-126): 28-Day Dietary Toxicity Study in CD-1 Mice. Project Number: 041161. Unpublished study prepared by Dow Chemical Co. 193 p.
47289128	Johnson, K.; Andrus, A. (2005) Dinocap II (DE-126): 90-Day Dietary Toxicity Study in CRL: CD (SD) IGS BR Rats. Project Number: 041157. Unpublished study prepared by Dow Chemical Co. 447 p.
47289129	Stebbins, K.; Brooks, K.; Lacher, J. (2005) Dinocap II (DE-126): 90-Day

MRID	Citation
	DietaryToxicity Study in Beagle Dogs with a Dinocap Comparative Control and a 1-Year Dinocap II Satellite Group-Interim Report. Project Number: 041148. Unpublished study prepared by Dow AgroSciences LLC. 415 p
47289130	Stebbins, K.; Brooks, K.; Lacher, J. (2006) Dinocap II (DE-126): 90-Day DietaryToxicity Study in Beagle Dogs with a Dinocap Comparative Control and a 1-Year Dinocap II Satellite Group-Final Report. Project Number: 041148A. Unpublished study prepared by Dow AgroSciences LLC. 133 p.
47289131	Stebbins, K.; Brooks, K.; Lacher, J. (2006) Supplemental Report for Study ID 041148 - Dinocap II (DE-126): 90-Day DietaryToxicity Study in Beagle Dogs with a Dinocap Comparative Control and a 1-Year Dinocap II Satellite Group-Interim Report. Project Number: 041148S. Unpublished study prepared by Dow AgroSciences LLC. 14 p.
47289132	Carney, E.; Tornesi, B. (2005) Dinocap II (DE-126): Oral Gavage Developmental Toxicity Study in CD-1 Mice. Project Number: 040329. Unpublished study prepared by Dow AgroSciences LLC. 264 p.
47289133	Carney, E.; Tornesi, B. (2005) Revised Report for: Teratogenicity of Selected Dinocap Isomers in CRL:CD1 (ICR) Mice. Project Number: 051068. Unpublished study prepared by Dow AgroSciences LLC. 211 p
47289134	Carney, E.; Tornesi, B. (2005) Dinocap II (DE-126): Oral Gavage Developmental Toxicity Study in CD Rats. Project Number: 041128. Unpublished study prepared by Dow AgroSciences LLC. 366 p.
47289136	Carney, E.; Tornesi, B. (2005) Dinocap II (DE-126): Oral Gavage Developmental Toxicity Study in New Zealand White Rabbits. Project Number: 041127. Unpublished study prepared by Dow AgroSciences LLC. 356 p.
47289137	Mecchi, M. (2005) Salmonella escherichia coli; Mammalian Microsome Reverse Mutation Assay Preincubation Method with a Confirmatory Assay with Dinocap II (DE-126): Final Report. Project Number: 6736/148, 26949/0/42203CD. Unpublished study prepared by Covance Laboratories Inc. 35 p.
47289138	Seidel, S.; Schisler, M.; Kleinert, K. (2005) Evaluation of Dinocap II (DE-126) in the Chinese Hamster Ovary Cell / Hypoxanthine-Guanine-Phosphoribosyl Transferase (Cho/HGPRT) Forward Mutation Assay. Project Number: 041160. Unpublished study prepared by Dow AgroSciences LLC. 30 p.
47289139	Charles, G.; Schisler, M.; Kleinert, K. (2005) Evaluation of Dinocap II (DE-126) in an in vitro Chromosomal Aberration Assay Utilizing Rat Lymphocytes. Project Number: 041159. Unpublished study prepared by Dow AgroSciences LLC. 35 p. (001-260). Unpublished study prepared by Biosafety Research Center. 90 p.
47289140	Charles, G.; Grundy, J.; Schisler, M. (2005) Evaluation of Dinocap II (DE-126) in the Mouse Bone Marrow Micronucleus Test. Project Number: 041163. Unpublished study prepared by Dow AgroSciences LLC. 51 p.
47289141	Porter, D. (1996) Identification of 2,4-Dinitro-6-(1-Methylheptyl)Phenyl Crotonate Metabolites in Rat and Mouse Urine. Project Number: 95R/0064, 95P/064. Unpublished study prepared by Rohm and Haas Co. 94 p.
47289142	Honeycutt, R.; Gartska, T. (1976) The Identification of Metabolites of 2,4-Dinitro-6-(2-Octyl) Phenyl Crotonate in Rat Urine and Feces. Project Number: 3423/76/29. Unpublished study prepared by Rohm and Haas Co. 134 p.
47304900	Dow Agrosciences LLC (2007) Submission of Product Chemistry, Residue, and Toxicity Data in Support of the Application for Registration of Meptyldinocap and the Petition for Tolerance of Meptyldinocap for Use on Grapes. Transmittal of

MRID	Citation
	7 Studies.
47304901	Nelson, R. (2007) Product Chemistry Data Requirements for Import Tolerance for Meptyldinocap. Project Number: NAFST/07/150. Unpublished study prepared by Dow Agrosciences LLC and Dow Chemical Co., and Huntingdon Life Sciences, Ltd. 333 p.
47304902	Feilden, A.; Howie, D. (1999) To Determine the Magnitude of Residues of Dinocap During the Twenty Eight Days Following the Final Application in the Raw Agricultural and Processed Commodity of Wine Grapes Resulting from Sequential Directed Application of Karathane LC or Karathane FN57 in Germany and Northern France. Project Number: RAS/17, RAS/17/980214, ER/72/1/LC. Unpublished study prepared by Huntingdon Life Sciences, Ltd. 274 p.
47304903	Lees, M. (1998) To Determine the Magnitude of Residues of Dinocap During the Twenty Eight Days Following the Final Application in the Raw and Processed Agricultural Commodity of Grapes Resulting from Sequential Directed Application of Karathane LC in Germany. Project Number: R/H/204, R/H/204/973651. Unpublished study prepared by Huntingdon Life Sciences, Ltd. 250 p.
47304904	Class, T. (2002) Dinocap: Assessment and Validation of the Multi-Residue Enforcement Method DFG S19 (Extended Revision) for the Determination of Dinocap in Plant Material. Project Number: 021219, P/649/G, P/B/649G. Unpublished study prepared by PTRL Europe Gmbh. 57 p.
47304905	Honeycutt, R.; Garstka, T. (1976) The Decline of Karathane Residues in Squash. Project Number: 3423//76/3. Unpublished study prepared by Rohm & Haas Co. 127 p.
47304906	Brooks, K.; Golden, R. (2005) GF-1478: Acute Oral Toxicity Screening Studies in F344 and CD (SD) Rats. Project Number: 050413, DR/0395/1562/010. Unpublished study prepared by Dow Chemical Co., 12 p.
47304907	Rogers, J.; Carver, B.; Gray, L.; et al. (1987) The Developmental Toxicity of Dinocap in the Mouse is not Due to Two Isomers of the Major Active Ingredients. Project Number: 87RJ/2742. Unpublished study prepared by EPA / RTP. 15 p.
47602200	Dow Agrosciences Llc. (2008) Submission of Residue Data in Support of the Petition for Tolerance of Meptyldinocap for Use on Grape, Grape Juice and Wine. Transmittal of 1 Study.
47602201	Jones, G. (2006) Residues of Dinocap or DE-126 in Wine Grapes at Intervals and Harvest Following Multiple Applications of GF-1344 or GF-1478, Southern Europe-2005. Project Number: GHE/P/11347, AF/8928/DE, 10001049. Unpublished study prepared by Agrisearch UK, Ltd. 145 p.
47663000	Dow Agrosciences, LLC. (2009) Submission of Residue Data in Support of the Petition for Tolerance of Meptyldinocap for Use on Apples and Grapes. Transmittal of 1 Study.
47663001	Foster, D. (2002) Dinocap Method Validation: DNOPC and DNOP Validation of Methodology for the Determination of DNOPC and DNOP in Apples and Grapes Using LC-MS/MS (Replacement Study for MRID 47289107). Project Number: GH/C/5503, DOS/220/DOS/220/0229, DOS/220/022962. Unpublished study prepared by Huntingdon Life Sciences, Ltd. 76 p.