

MEPTYLDINOCAP (244)

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EXPLANATION

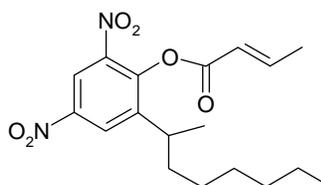
Meptyldinocap is a protectant and curative fungicide for the control of powdery mildew diseases. The meptyldinocap is the single isomer of the existing active substance dinocap. Dinocap had been evaluated several times by the JMPR from 1969. In 1992 the JMPR recommended withdrawal of the temporary MRLs of dinocap. Based on a new submission, the 1998 JMPR evaluated dinocap as a new compound.

At the Forty-first session of the CCPR (2009), meptyldinocap was scheduled for the evaluation as a new compound by 2010 JMPR.

The manufacturer submitted new information on residues in/on pome fruits, stone fruits, grapes, strawberries and curcurbits with edible and inedible peel.

IDENTITY

ISO common name:	Meptyldinocap (proposed)
IUPAC name:	2-(1-methylheptyl)-4,6-dinitrophenylbut-2-enoate
Chemical Abstract name:	(E)-2-butenic acid, 2-(1-methylheptyl)-4,6-dinitrophenyl ester.
CAS No.:	131-72-6
CIPAC No.:	Not available
Synonyms:	2,4-dinitro-6-(1-methylheptyl)phenyl crotonate; DE-126, RH-23163
Molecular Formula:	C ₁₈ H ₂₄ N ₂ O ₆
Structural Formula:	



Molecular Weight:	364.40
Minimum purity	900 g/kg

The meptyldinocap is the single isomer [2,4-dinitro-6-(1-methylheptyl)phenyl crotonate] of the existing active substance dinocap, which is a mixture of 2,4-dinitro-6-octylphenyl crotonates and 2,6-dinitro-4-octylphenyl crotonates. The 'octyl' being a mixture of 1-methylheptyl, 1-ethylhexyl and 1-propylpentyl groups. Approximately 22% of dinocap is meptyldinocap.

The 2010 JMPR evaluated studies which were conducted with meptyldinocap and dinocap. The single isomer, meptyldinocap is often referred to as 2,4-DNOC and 2,4-dinitro-6-(2-octyl)phenyl crotonate in original studies. The typical composition of the test substances are given below:

Isomers	Meptyldinocap	Dinocap
Meptyldinocap, 2,4-dinitro-6-(1-methylheptyl)phenyl crotonate	98.5%	22%
2,6-dinitro-4-(1-methylheptyl)phenyl crotonate	0%	11%
2,4-dinitro-6-(1-ethylhexyl)phenyl crotonate a	1.5%	22%
2,6-dinitro-4-(1-ethylhexyl)phenyl crotonate	0%	11%
2,4-dinitro-6-(1-propylpentyl)phenyl crotonate	0%	22%
2,6-dinitro-4-(1-propylpentyl)phenyl crotonate	0%	11%

^a The compound is considered as an impurity in technical meptyldinocap, which contains only one isomer as an active ingredient.

PHYSICAL AND CHEMICAL PROPERTIES

Pure and Technical Active Ingredient (Purity in bracket)

Chemical/physical properties	Results	References	
Appearance (92.9 and 97.2%)	Yellow to orange/brown liquid	Ardern 1997, Nelson 2005 a and b	
Melting point (> 95%)	-22.5 °C		
Relative density (> 95%)	D ₄ ²⁰ = 1.11		
Solvent solubility, 20 °C (> 95%)	Acetone	> 252 g/L	Betteley 1994, Betteley 1997a and b, Betteley 2001a and b
	1,2-Dichloroethane	> 252 g/L	
	Ethyl acetate	> 256 g/L	
	n-Heptane	> 251 g/L	
	Methanol	> 253 g/L	
Xylene	> 256 g/L		
Water solubility, 20 °C (97.1, with radio-labelled isomers at 98.9 and 95.4%)	1.51 × 10 ⁻⁴ g/L	at 20 °C (pH 5.0)	
	2.48 × 10 ⁻⁴ g/L	at 20 °C (pH 7.0)	
Vapour pressure (99.3%)	7.92 × 10 ⁻⁶ Pa at 25 °C		
Volatility, Henry's Law Constant @ 20 °C (99.3%)	1.16 × 10 ⁻² Pa m ³ mol ⁻¹		
Partition coefficient, 20 °C and pH 7 (97.1% radio-purity)	log P _{ow} = 6.55 at 20.5 °C (pH 7)		
Dissociation constant (NA)	As the substance is an ester and the chemical structure of the molecule contains no moiety which could dissociate or add protons, the determination of the pKa is not necessary.		
Hydrolysis	The hydrolytic stability of 2,4-DNOPC in the dark at 20 °C showed DT ₅₀ values of 447 days at pH4, 229 days at pH5, 56 and 30 days at pH7, and 0.7 and 9.3 days at pH 9. At 30 °C the DT ₅₀ values were 91.4, 30.5 and 2.34 days, respectively. The only metabolite		

Chemical/physical properties	Results	References
	identified was 2,4-DNOP occurring at levels > 10%. Parent compound amounted to > 80% at 35 days with total recovery of radioactivity > 96%	
Quantum yield	Based on an aqueous photolysis study conducted with a Xenon arc lamp using meptyldinocap uniformly labelled with carbon-14 in the phenyl ring, at a concentration of 1 µg/ml. The quantum yield for photo degradation of meptyldinocap was 0.24%.	Randazzo, DJ, 1995

FORMULATIONS

Meptyldinocap is available in the following formulation.

Formulation	Active ingredient content	Common Trade Names
Emulsifiable concentrate (EC), containing only <u>meptyldinocap</u> as the active ingredient	350 g/L meptyldinocap (GF-1478)	Karathane Star, Karathane Gold

The supervised trials considered by the present Meeting used the 350 g/L EC formulation containing either meptyldinocap or dinocap.

METABOLISM AND ENVIRONMENTAL FATE

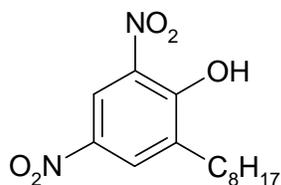
Animal metabolism

The intended use for meptyldinocap is on vines, cucurbits and strawberries, which are not fed to animals. Therefore, no animal metabolism studies were provided for evaluation.

The 1998 JMPR evaluated an early study in which caws were dosed with dinocap at 0.1, 0.3 and 1 ppm level in the diet. The main route of elimination was with faeces with small amounts in the urine. The sensitivity of detection of radioactivity was 0.004 mg/kg in milk and urine, 0.05 mg/kg in fat and 0.04 mg/kg in other tissues. No radioactive residues were detectable in milk or tissues at any dose level (FAO Pesticide Residues in Food, Report 1998, FAO Plant Production and Protection Paper 148, p.100).

Plant metabolism

The plant metabolism studies submitted to the current meeting were also evaluated by the 1998 JMPR. The metabolism studies were carried out with meptyldinocap [2,4-dinitro -6-(2-octyl)phenyl crotonate] on apples, cucumbers and squash. A single major metabolite (2,4-dinitro-6-(2-octyl) phenol) was identified and referred to as 2,4-DNOP.



2,4-DNOP (mw 296)

Apples

An apple tree was treated with a single foliar application of an EC formulation containing 45.6% ai at a rate equivalent to 1.96 kg ai/ha, four times the normal maximum application rate (0.49 kg ai/ha). (Dohmeier, 1993). The test material was applied using a compressed air sprayer. At the time of application, the tree bore fruit with an average diameter of approximately 5 cm; by the time of the final harvest, (twenty one days later), the apple fruit was approximately 6 cm in diameter. Apples and leaves were harvested from treated and control trees on the day of application, both before and after treatment, and after 7, 14, and 21 days. The samples were stored frozen for one year before analysis. Half of each fruit sample was analysed as whole fruit, and the other half peeled, and the peel and pulp analysed separately. The total radioactivity in the samples was determined by combustion with the results shown in Table 1.

Table 1 Radioactivity in apples treated with meptyldinocap

PHI	¹⁴ C mg/kg as meptyldinocap				
	Whole fruit	Pulp	Peel	Pulp + peel	Leaves
0	1.37	0.25	16.7	2.9	195
7	2.38	0.13	12.8	2.3	113
14	1.67	0.15	12.97	2.2	76.3
21	1.57	0.12	10.1	1.57	70.6

The samples were extracted with methanol which recovered more than 90% of the radioactivity from the day 0 samples, and 40–60% from the aged samples. More than 92% of the radioactivity at each PHI was associated with the peel. When the residues extracted by methanol were partitioned with hexane and ethyl acetate most of the radioactivity (80–90%) passed into the hexane. An additional 30–45% of the total radioactivity in the aged fruit samples could be released with 0.1 M NaOH in methanol. After adjusting the pH of the extract 80–95% of this radioactivity could be partitioned into ethyl acetate. The total radioactivity recovered in the neutral and alkaline methanolic extracts was more than 80% in all cases. The results are shown in Table 2.

Table 2 Distribution of ¹⁴C-meptyldinocap residues in extracts of apple peel and whole apples.

Fraction/extract	% of total radioactivity at days after last treatment							
	0		7		14		21	
	Peel	Whole fruit	Peel	Whole fruit	Peel	Whole fruit	Peel	Whole fruit
Hexane/MeOH	88.1	91.8	41.6	46.2	26.3	25.7	20.2	25.2
EtOAc/MeOH	8.2		14.1	10.2	12.1	11.8	11.3	10.3
Aqueous/MeOH	0.4	0.4	3.8	5.3	6.3	5.4	8.3	9.6
EtOAc/MeOH NaOH		–	31.7	19.0	41.1	40.1	45.1	32.5
Aqueous/MeOH/NaOH			1.3	2.0	2.1	2.3	2.3	8.1
Post-extraction solid	3.3	2.8	7.5	9.1	12.1	14.3	12.8	13.2

Peel samples were analysed six months after the whole fruit, showing that the nature of the residues did not change dramatically during storage.

The parent meptyldinocap and the metabolite 2,4-DNOP were identified in the hexane and ethyl acetate fractions of the fruit extracts by TLC and reverse phase HPLC. The parent decreased from 73% of the total radioactivity at day 0 to 23% at day 7, 11% at 14 and 8% at 21 days.

Table 3 Residues of meptyldinocap and its metabolites in apple fruit and leaves

PHI, days	Meptyldinocap		2,4-DNOP
	mg/kg	TRR%	mg/kg
0	2.12	73	0.06
7	0.52	23	0.08
14	0.25	11	0.05
21	0.12	7.7	0.03

The half-life of meptyldinocap was 5.2 days, showing that it was rapidly degraded on the fruit surface. The phenol metabolite was present at low concentrations, (2–4% of the total radioactivity at all sampling intervals), and appeared to be quickly metabolized to many polar compounds, none of them individually accounting for more than 7% of the total radioactivity. They could not be identified.

An additional study was conducted to provide information on the identity of the unidentified metabolites of meptyldinocap in apples (Dohmeier, 1994). The test substance was meptyldinocap, uniformly labelled with ^{13}C and ^{14}C in the phenyl ring, applied to a single apple tree as an EC formulation at a rate of 1.96 kg ai/ha.

Apple peel samples were extracted three times with MeOH in a blender and the extract was partitioned with hexane. The post-extraction solids were treated with methanolic NaOH solution to release additional radioactivity. After acidification, the methanolic base extract was partitioned with ethyl acetate. The hexane fraction was cleaned up by silica gel chromatography and the residues eluted with increasing concentrations of methanol in methylene chloride. Fractions containing radioactivity but not meptyldinocap or 2,4-DNOP were methylated and fractionated by TLC and HPLC and the purified components analysed by GC-MS. The resulting mass spectra allowed tentative structures to be proposed for five minor metabolites: [2-methyl-5-nitro-7-(2-octyl) benzoxazole, 2-(hydroxymethyl)-5-nitro-7-(2-octyl) benzoxazole, 4-(1-propenyl)-5-nitro-7-(2-octyl)benzoxazole, 5-nitro-7-(octyl) benzoxazole and 2-hydroxymethyl-5-nitro-(2-octyl)-phenyl crotonamide.

A portion of the post-rinsed tissue was sequentially analysed beginning with a neutral extraction, then an acid hydrolysis followed by acetonitrile extraction. Immature and mature samples were then subjected to bound residue determinations such as acid detergent fibre, and lignin isolation. Finally, a methanolic KOH digestion proved the "lignin" to more probably be composed of ^{14}C -cutin. None of these metabolites amounted to more than 0.5% of the total residue (Dohmeier, 1994).

As photolysis was identified as a possible degradation pathway for meptyldinocap on the apple surface (Byrne, 2003), a mixture of ^{14}C - and ^{13}C -labelled meptyldinocap was irradiated with a Hanau "Sun test" lamp for 26 hours. The photolysis products were methylated and cleaned up on Florisil column and by TLC and HPLC. The isolated products were analysed by GC-MS, and their spectra compared with the spectra of the metabolites isolated from apple peel. The two metabolites identified in apple peel were also identified as photoproducts. The identified metabolites of meptyldinocap in apples is shown in Figure 1

Meptyldinocap

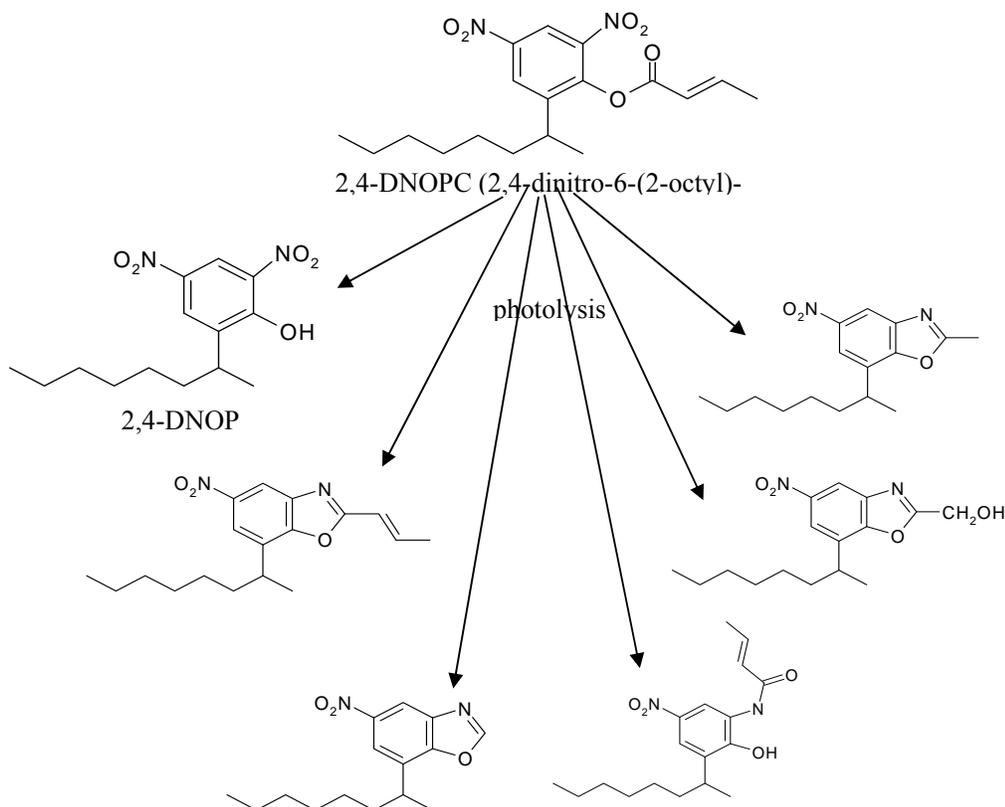


Figure 1 Metabolites of meptyldinocap identified in apple

Cucumbers

The distribution and rate of the decrease of residues after a single treatment with ^{14}C -meptyldinocap at 0.56 kg ai/ha were studied (Honeycutt, 1976a). Blossoms were just starting to appear on the plants at the time of application. The cucumber plants were allowed to grow thickly and three or four whole plants were taken at 0, 8, 21, 34, 48, and 63 days after treatment. Immature fruit samples were taken starting at 21 days after treatment and mature fruit was harvested at 48 and 63 days.

The residues of ^{14}C -DNOPC dissipated rapidly from the cucumber leaves and stems.

Table 4 Residues in cucumbers treated with ^{14}C -meptyldinocap.

PHI	Residues, mg/kg as meptyldinocap						
	Leaves	Stems	Flowers	Immature fruit	Mature Fruit		
					Peel	Pulp	Whole
0	38.2	3.6	—	—			
8	28.9	3.9	5.4	—			
21	4.1	0.7	1.0	1.0			
34	2.5	0.6	0.5	—			
48	1.1	0.4		0.2	0.15	0.11	0.16
63	1.4	0.5					0.09

The half lives of radioactive residues on leaves and stems were 11.8 days and 18.8 days, respectively. The ^{14}C residues on the leaves decreased from 38.2 mg/kg immediately after application to 1.4 mg/kg at final harvest. The ^{14}C residues in the stems decreased from 3.6 mg/kg immediately after application to 0.5 mg/kg at final harvest. The ^{14}C residues in the flowers decreased from

5.4 mg/kg eight days after application to 0.5 mg/kg 34 days after application. The whole mature fruit harvested 48 days after application contained ^{14}C residues of 0.16 mg/kg and whole mature fruit harvested 63 days after application contained 0.09 mg/kg. Of the whole mature fruit harvested 48 days after application, the peels contained 0.15 mg/kg and the flesh contained 0.11 mg/kg. Of the residues extracted from the leaves by acetone, only one metabolite (2,4-DNOP) occurred in significant (> 10%) quantities.

Cucumber leaves from day 8 were analysed by TLC for metabolites. Twenty eight metabolites were detected but only the parent compound and DNOP were identified.

Table 5 Relative levels of meptyldinocap and metabolites in cucumber leaves after 8 days.

Metabolite	% of extractable residue	% of total residue
Two unidentified	0.9	0.4
meptyldinocap	0.7	0.3
2,4-DNOP	5.7	2.4
Unidentified	19.4	8.2
Unidentified	3.9	1.6
Unidentified	3.1	1.3
12 polar metabolites	66.1	27.8
Unextracted	–	58.0

Cucumbers harvested at 48 and 63 days were extracted with acetone and the post-extraction solid analysed by combustion and radio-assay. The acetone extract was redissolved in acetone/water and partitioned twice with methylene chloride. The organic phases were combined and concentrated to dryness, and the residue redissolved in petroleum ether/methylene chloride. The concentrated extract was analysed by TLC and radioactive bands quantified by LSC. Ninety three percent of the residue at harvest was contained in unidentified water soluble or non-extractable materials. (Honeycutt, 1976a). The results are shown in Table 6.

Table 6 Relative levels of meptyldinocap and metabolites in cucumbers after 48 and 63 days

Compound or fraction	% of total ^{14}C	
	48 days	63 days
meptyldinocap	0.7	3.5
2,4-DNOP	0.6	4.5
Unidentified	0.9	1.3
Unidentified	0.6	0
Unidentified	0.4	1.5
Unidentified	0.6	2.3
Unidentified	0.9	3.3
Unidentified	1.1	3.8
Polar metabolites	1.4	5
Aqueous fraction	40	35
Unextracted	52	40

Cucumber fruit which contained 0.1 mg/kg ^{14}C residues at 48 days contained a small amount of parent DNOPC and at least five organic soluble metabolites, all of which amounted to 7% of the residues in the cucumbers at harvest. Ninety three percent of the residues at harvest was contained in unidentified water soluble or non-extractable materials.

In another study ^{14}C -meptyldinocap was applied post-emergence to a plot of cucumbers at the beginning of blossoming stage. Samples of leaves, stems, fruit, and soil were taken periodically and analysed for radioactive residues (Honeycutt, RC & Garstka, TA, 1976 TR 3423-76-2). Cucumber leaves were extracted with acetone and analysed by thin layer chromatography for metabolites of ^{14}C -DNOPC.

The residues of ^{14}C -DNOPC dissipated rapidly from cucumber leaves and stems. The half-life for ^{14}C residues of ^{14}C -DNOPC on cucumber leaves in the field was about 12 days. The parent compound amounted to only 0.3% of TRR at day 8 after treatment.

The metabolism of ^{14}C -DNOPC in cucumber leaves was extensive, leading to 18 minor metabolites. Only 2,4-DNOP could be identified amounting to 2.4% of TRR at day 8, while the unextractable residues accounted for 58% of TRR.

Squash

Formulated ^{14}C -meptyldinocap was applied two times at a rate of 0.56 kg ai/ha to two rows of squash. The squash plants were in bloom at the time of the first treatment. Whole plants were sampled 0, 7, 17, 25, 32, 40, 53, 66 and 80 days after the first application (0, 8, 15, 23, 36, 49 and 63 days after the final application). Fruit samples were taken from 15 days after the final application. Samples were assayed for radioactivity by combustion and LSC (Honeycutt and Garstka, 1976d). The results are shown in Table 7.

Table 7 Residues in squash treated three times post-emergence with ^{14}C -meptyldinocap.

Days after 1st treatment	^{14}C , mg/kg as 2,4 DNOPC					
	Leaves	Root and stems	Immature whole fruit	Mature fruit		
				Peel	Pulp	Whole
0	4.2					0.14
7 (after 2 nd treatment)	44.0	8.2				0.36
17 (after 3 rd treatment)	34.8	3.1				0.11
25	17.5	3.3				0.35
32	12.2	1.9		0.58	0.15	0.25
40	11.9	1.8	0.19	0.08	0.21	
53	4.2	1.5	0.02	0.70	0.19	0.09
66	2.7	0.7	0.04	0.15	0.06	0.18
80	1.7	0.7	0.06			

The half-life of the radioactivity in the leaves was 8 days. The leaves sampled at this time were extracted twice with benzene, and the fruit twice with acetone. The fruit extract was partitioned three times with petroleum ether/methylene chloride, and the organic phases combined and dried with sodium sulphate. The organic and aqueous phases from the fruit extraction were radio-assayed. The organic extracts from the leaves and fruit were concentrated and analysed by TLC. Radioactive bands on the TLC plates were visualized by autoradiography. The radioactivity was eluted from each band with acetone or methanol and the eluates radio-assayed.

2,4-DNOP was the main metabolite in the leaves and was also found in the fruit. About six unidentified metabolites were found in the fruit and 10 in the leaves, none of which individually accounted for more than 10% of the TRR. The distribution of radioactivity in the fruit and leaves 8 days after the last treatment is shown in Table 8. The 2,4-DNOP, meptyldinocap, organic soluble metabolites and water soluble polar metabolites and unextractable ^{14}C -residues amounted to 1.3%, 5.9%, 5.5%, 21% and 57.6% of TRR, respectively.

^{14}C -meptyldinocap was applied in an EC formulation post-emergence to squash being at the beginning of blossoming stage (Honeycutt, RC, 1993. Report No. 3423-76-33) Within 5 minutes of spraying, twelve large squash leaves were covered with aluminium foil to provide dark controls. Two 30 cm² aluminium foil covered boards as well as two 30 cm² pieces of plexiglass (U.V. transparent) were immediately placed on the treated soil at the end of each row of the squash.

Leaf samples were taken at regular intervals up to 74 hours, rinsed with benzene, and the resulting extracts were analysed for leaf photoproducts by thin layer chromatography (TLC). It was found that meptyldinocap photolysed rapidly and extensively on leaf surfaces (Table 7) while on soil the photolysis of meptyldinocap was much slower and less extensive.

It was concluded that photolysis will play a major role in the rapid dissipation of this fungicide from plant foliage (half-life of 8 days). The slow and incomplete photolysis of meptyldinocap on soil may explain why the parent compound dissipates more slowly from soil (half-life 61 days) than it does from plants.

Table 8 Percentage of ¹⁴C Recovered from TLC Plate

Photo products	0	27 hours dark	27 hours light
meptyldinocap	92	93	39
Polar photoproducts	3	2	53

Environmental fate in soil

Soil metabolism, degradation, leaching and rotational crop studies are not required for compounds with intended use of foliar application only on permanent crops with no crops planted in rotation (JMPR Manual 2nd.ed 3.2.3.3 section).

As part of the plant metabolism studies soil samples were also taken and analysed for meptyldinocap residues.

The distribution and rate of decrease of residues after a single treatment of a cucumber field with ¹⁴C-meptyldinocap at 0.56 kg ai/ha were studied. (Honeycutt, 1976a). Soil core samples were taken at three different places in the plot on each sampling date. The soil sections taken at 0–2.5 cm, 2.5–7.6 cm, and 7.6–15.2 cm depths were pooled.

The ¹⁴C residues in the top 2.5 cm of soil decreased from 0.45 mg/kg immediately after application to 0.31 mg/kg after 63 days. The ¹⁴C residues in the 2.5–7.6 cm soil depth never exceeded 0.02 mg/kg and the 7.6–15.2 cm soil depth residues never exceeded 0.007 mg/kg.

In another study ¹⁴C-meptyldinocap was applied post-emergence to a plot of cucumbers. Samples of soil were taken periodically and analysed for radioactive residues (Honeycutt, RC & Garstka, TA, 1976 TR 3423-76-2). The residues of ¹⁴C-DNOPC in the soil in which the cucumbers were grown dissipated at a much slower rate than from the cucumber plants. Furthermore, there appeared to be no significant leaching of the ¹⁴C-DNOPC residues into the lower depths of the soil.

Formulated ¹⁴C-meptyldinocap was applied three times at a rate of 0.56 kg ai/ha to two rows of squash (Honeycutt and Garstka, 1976d) The squash plants were in bloom at the time of the first treatment. Samples were taken 0, 8, 15, 23, 36, 49 and 63 days after the final application. Soil cores taken at three different places in the plot at each sampling were sectioned in 0–2.5, 2.5–7.6, and 7.6–15.2 cm depths and the three sections at each depth pooled.

The ¹⁴C residues in the top section of the soil (0–2.5 cm) decreased from 0.43 mg/kg after the last treatment to 0.40 mg/kg 63 days later. The ¹⁴C residues in the other soil sections were low.

The residues of ¹⁴C-DNOPC in the soil in which the squash were grown dissipated at a much slower rate than from the squash plants. There appeared to be no significant leaching of ¹⁴C-DNOPC residues into the lower depths of the soil.

¹⁴C-meptyldinocap) was applied in an EC formulation post-emergence to squash (Honeycutt, RC, 1993. Report No. 3423-76-33) Within 5 minutes of spraying, two 30 cm² aluminium foil covered boards as well as two 30 cm² pieces of plexiglass (U.V. transparent) were immediately placed on the treated soil at the end of each row of the squash.

Surface samples of soil (6 mm thick) were taken at several time intervals, Soxhlet extracted with benzene, and the extracts also analysed for soil photoproducts by TLC. It was found that the photolysis of meptyldinocap was much slower on soil surfaces and less extensive than on leaves.

The slow and incomplete photolysis of meptyldinocap on soil may explain why it dissipates more slowly from soil (half-life—61 days) than it does from plants.

The results of the studies with cucumber and squash are similar and indicate that low levels of residues would be available within the root zones of rotated crops.

Metabolism in Rotational Crops

The reports evaluated by the 1998 JMPR indicated that when beans, oats and turnips were grown in soil in which cucumber and squash were treated with ¹⁴-C meptyldinocap 250 days earlier, the radioactive residues in samples taken until maturity of the crops were at or below 0.02 mg/kg.

METHODS OF RESIDUE ANALYSIS**Analytical methods for plant matrices**

The analytical method used for determining meptyldinocap residues had also been used for the determination of dinocap residues in supervised trials.

The analytical methods were developed and validated for the determination of dinocap residues which consists of two isomer groups of 2,4-dinitro-6-octylphenyl crotonate (mixture of 3 isomers: 2,4-dinitro-6-(1-methyl heptyl)-phenyl crotonate, 2,4- dinitro-6-(1-ethyl hexyl)-phenyl crotonate and 2,4-dinitro-6-(1-propyl pentyl)-phenyl crotonate) and 2,6-DNOPC (mixture of 3 isomers: 2,4-dinitro-4-(1-methyl heptyl)-phenyl crotonate, 2,6- dinitro-4-(1-ethyl hexyl)-phenyl crotonate and 2,6-Dinitro-4-(1-propyl pentyl)-phenyl crotonate). Following the solvent extraction, the residues were converted to the corresponding phenols and determined by GC after methylation with diazomethane or analysed directly by HPLC-MS/MS.

In the case of method DOS/220-01R, the analytes were extracted from the matrix with acetone:methanol:4 N hydrochloric acid mixture followed by a liquid:liquid partition using hexane:ethyl acetate. The analytes were hydrolyzed to their corresponding phenols. Final clean-up was by a liquid:liquid partition using ethyl acetate. Quantitation was performed using liquid chromatography with tandem mass spectrometric detection (Munro, S, 2002]. The 3 isomers of 2,4 DNOP and 2,6-DNOP (1 methylheptyl, 1-ethylhexyl and 1-propylpentyl) were not fully separated and the peak area of isomer groups were added together for quantitation. The method was validated by analysis of fortified samples for residues of dinocap isomers in apples and grapes over the range of 0.05–1.0 mg/kg. The limit of quantitation (LOQ) for apples and grapes is 0.05 mg/kg (0.025 mg/kg for each isomer group or for 2,4-DNOP in case of meptyldinocap) for both DNOPC and DNOP. The method was independently validated (Cordon, C, 2002)

Table 9 Summary of recoveries from fortified apple and grape samples

Fortification level (mg/kg)	% Recovery	
	DOS/220-01R	Independent validation
APPLES (DNOPC)		
0.05	86, 75, 90, 77, 73	89, 98, 88, 95
1.0	82, 84, 86, 85, 77	101, 97, 89, 106, 109
Mean	82	97
Mean control values (mg/kg)	0	0.0032
% RSD over the validated range	6.9	7.8
APPLES (DNOP)		
0.05	79, 91, 92, 96, 98	73, 72, 84, 78, 81
1.0	105, 85, 97, 92, 94	93, 77, 79, 78, 78
Mean	93	79
Mean control values (mg/kg)	0	0.0026
% RSD over the validated range	7.7	7.5
GRAPES (DNOPC)		
0.05	77, 72, 83, 81, 92	88, 91, 65, 88, 74,
1.0	73, 83, 84, 81, 77	78, 83, 89, 66, 87
Mean	80	81
Mean control values (mg/kg)	0	0.0011
% RSD over the validated range	7.3	11.9
% RSD over the lowest validated range (0.01 mg/kg)	9.2	13.8

Fortification level (mg/kg)	% Recovery	
	DOS/220-01R	Independent validation
GRAPES (DNOP)		
0.05	73, 82, 81, 83, 70	72, 80, 77, 86, 83
1.0	82, 86, 86, 88, 91	84, 75, 67, 92, 85
Mean	82	80
Mean control values (mg/kg)	0	0.0009
% RSD over the validated range	7.9	9.3
% RSD over the lowest validated range (0.mg/kg)	7.6	6.8

Apples

Residues were Soxhlet extracted from the apples by overnight extraction with methanol. The dinocap isomers were converted to phenols by basic hydrolysis. The extract was partially purified by a hexane partition. The extract was acidified with hydrochloric acid and then partitioned again with hexane. The hexane was dried over sodium sulphate and taken to dryness. The residue was taken up in ethyl ether and the phenols were methylated with diazomethane. The solvent was evaporated to dryness and further cleaned up with silica gel column chromatography. Quantitation of the methylated phenols was performed by gas chromatography with a capillary column and a capillary thermionic specific detector optimized for nitrogen. The mean recovery in the 0.025-0.25 mg/kg concentration level was 89% with relative standard deviation of 11% (n = 15). The LOQ of the method for the mixture of isomers was 0.05 mg/kg. (Analytical Method for the Determination of Dinocap Residues in Apples, TR 34-91-19, (Brackett, CK, 1991).)

The DFG S-19 multi residue method was slightly modified (GH-C 5610, Class, T, 2002) by applying different extraction modes and elution sequences for different types of sample materials:

Sample material	Extraction	Cleanup	Detection
White table grape (high water content)	1 st : acetone+ water 2 nd : ethyl acetate/cyclohexane	GPC + silica gel columns	GC/ECD
Apple (acidic material)	1 st : NaHCO ₃ to adjust pH, acetone 2 nd : ethyl acetate/cyclohexane	GPC + silica gel	GC/ECD
Barley (dry material)	1 st : soak in water adding acetone 2 nd : ethyl acetate/cyclohexane	GPC + silica gel columns	GC/ECD
Soya bean four (oily material)	1 st : Celite, acetone and acetonitrile Solvent replaced with isooctane	Silica gel column	GC/ECD

Table 10 The recoveries obtained with modified S-19 method for total dinocap

Fortification level (mg/kg)	% Recovery		
	Original Method Number DFG S19	Independent validation Dinocap	Independent validation meptyldinocap
WHITE TABLE GRAPES			
0.05	80, 84, 71, 79, 81		
1.0	78, 77, 88, 74, 85		
Mean	80		
Mean control values (mg/kg)	0		
% RSD over the validated range	6		
BARLEY GRAIN			
0.05	69, 91, 86, 81, 105	102, 100, 95, 92, 90	91, 97, 104, 121, 109

Fortification level (mg/kg)	% Recovery		
	Original Method Number DFG S19	Independent validation Dinocap	Independent validation meptyldinocap
1.0	78, 90, 99, 86, 96	78, 72, 79, 71, 96	111, 101, 100, 105, 95
Mean	88	87	104
Mean control values (mg/kg)	0	0	0
% RSD over the validated range	12	13	8
APPLE			
0.05	108, 91, 95, 89, 91	72, 87, 94, 76, 75	81, 95, 83, 103, 94
1.0	85, 86, 86, 85, 87	119, 104, 120, 120, 112	103, 109, 111, 102, 118
Mean	90	98	100
Mean control values (mg/kg)	0	0	0
% RSD over the validated range	8	20	12
SOYA BEAN FLOUR			
0.05	86, 89, 80, 92, 94	89, 90, 84, 87, 72	117, 97, 106, 117, 112
1.0	91, 78, 79, 83, 98	101, 107, 120, 91, 101	85, 78, 72, 84, 85
Mean	87	94	95
Mean control values (mg/kg)	0	0	0
% RSD over the validated range	8	14	18

The applicability of the method was also verified for pure meptyldinocap together with dinocap isomer mixture (Robaugh, DA & Arbaugh, S, 2007, Report No. 256431). The meptyldinocap peak was well separated from the dinocap isomers under the gas chromatographic conditions applied. The resulting average recoveries obtained from five replicate analyses are summarised below.

Table 11 Recoveries obtained with independent validation of DFG S-19 method based on EC detection

Compound	Added amount mg/kg	Matrix		
		Apples	Barley grains	Soya flour
Dinocap	0.05	81 ± 9%	96 ± 5%	85 ± 7%
	1.0	115 ± 7%	79 ± 10%	104 ± 20%
Meptyldinocap	0.05	91 ± 9%	105 ± 12%	110 ± 9%
	1.0	109 ± 6%	103 ± 6%	81 ± 6%

In addition to the independent validation of the GC/ECD quantitative method, a confirmatory method using GC/MS with negative chemical ionization was developed and validated. The average recoveries were similar to those obtained with ECD.

Mangoes

An analytical method was developed for the quantitative determination of meptyldinocap as 2,4-dinitrooctylphenyl (2,4-DNOP) in mangoes and soil using liquid chromatography tandem mass spectrometry (LC-MS/MS) (Kantar B, 2010). The method comprised an extraction with an acetone:methanol:4 N HCl (100:10:5, v/v/v) mixture followed by hydrolytic conversion of parent meptyldinocap to the corresponding phenol metabolite (2,4-DNOP), and cleanup was done by liquid: liquid partition using ethyl acetate. Final quantitation was performed by LC-MS/MS of 2,4-DNOP with negative electrospray ionization using gradient elution. The method was validated at concentrations ranging from 0.025 to 2 mg/kg, and the limit of quantification (LOQ) of meptyldinocap in mango and soil samples was 0.025 mg/kg. The recovery of meptyldinocap from mango and soil samples spiked at different levels with analytes found to be 93–98%, and the relative standard deviation for repeatability (RSDr) and reproducibility (RSDR) were acceptable (2–6%).

Stability of residues in stored analytical samples*Apples and grapes*

The stability of residues was tested in apples and grapes using 97.5% pure 2,4-DNOPC isomers and 2,6-DNOPC(iso) isomers in separate sets of trials (Gillis, NA, 1995). The meptyldinocap analytical standard contained 2,4-dinitro-6-(1-methyl heptyl)-phenyl crotonate, 2,4- Dinitro-6-(1-ethyl hexyl)-phenyl crotonate, and 2,4-Dinitro-6-(1-propyl pentyl)-phenyl crotonate.

On each occasion of analysis three untreated control sub-samples and two sub-samples fortified at 1.0 mg/kg, for each matrix, were selected at random and removed from storage. Two control samples for each matrix were freshly fortified at 1.0 mg/kg just prior to analysis, and the five samples for each matrix were analysed as a batch. The test portions were extracted with methanol. The dinocap isomers were hydrolysed with sodium hydroxide and after acidification partitioned with hexane. The dried extract was taken up in diethyl ether and methylated with diazomethane and detected with GC/ECD.

The results are summarised in the table below.

Table 12 Stability of dinocap residues in grapes after frozen storage

Matrix	Fortification level (mg/kg)	No. of months in frozen storage	Procedural Mean Recovery%	Mean Residue remained % ^a
Apples	1.0	0	93.5	87
	1.0	1	90	85.5
	1.0	3	93.5	72
	1.0	6	97	68
	1.0	9	79	73
	1.0	12	71.5	58
	1.0	18	81.5	68.5
	1.0	24	102.5	60
Grapes	1.0	0	95.5	88.5
	1.0	1	90	87.5
	1.0	3	90	89.5
	1.0	6	98	96.5
	1.0	12	96.5	108
	1.0	18	88.5	77
	1.0	24	103	81.5

^a The results are not corrected for the corresponding mean procedural recovery.

The overall mean procedural recovery and the portion of residues remaining in grapes were 94.5% and 89.8% respectively with standard deviations of 5.26% and 10.13%, indicating only a very slight decline of dinocap residues in grapes over a period of 24 months. The overall mean procedural recovery and the portion of residues remaining in apples were 88.6% and 71.5% respectively, with standard deviations of 10.34% and 10.52%, indicating a more marked decline of dinocap residues in apples over a period of 24 months.

In another study the storage stability in cucumbers, tomatoes, peaches, apples and strawberries were determined (Howie, D & Lees, M, 1999) The sub-samples were removed from the deep-frozen untreated homogenised materials and spiked individually with standard grade isomer mixtures of meptyldinocap(iso) and 2,6- DNOPC isomers at 1.0 mg/kg level.

The method of analysis for all matrices involved extraction by blending with methanol followed by basic hydrolysis using sodium hydroxide solutions. The extracts were then purified by liquid-liquid partition into hexane and methylated using diazomethane solutions. The extracts were further purified using silica gel column chromatography. Quantitation of the residues, following extract concentration, was by gas chromatography using an electron capture detector. The peaks of six

isomers were separated under GC conditions, but the individual isomers were not identified. The total dinocap concentration and recoveries were reported. The chromatograms indicate some variations in peak height ratios in stored samples compared to the ratios in analytical standards. The LOQ was 0.05 mg/kg.

Table 13 Stability of dinocap residues in apples, cucumbers, peaches, strawberries and tomatoes after frozen storage for 24 months ^a

Storage period [month]	0	1	3	6	9	12	18	24
Cucumber								
Mean procedural Rec. [%]	101	81	94	94	89	85	83	73
Mean portion remained [%]	95	94	102	105	101	104	88	86
Tomatoes								
Mean procedural Rec. [%]	102	85	93	72	86	86	87	80
Mean portion remained [%]	94	96	104	82	97	102	97	88
Peaches								
Mean procedural Rec. [%]	99	87	95	90	92	91	82	79
Mean portion remained [%]	96	92	96	98	105	96	87	84
Apples								
Mean procedural Rec. [%]	82	91	87	91	93	88	78	86
Mean portion remained [%]	81	89	81	107	105	100	99	95
Strawberries								
Mean procedural Rec. [%]	99	81	76	91	92	89	88	81
Mean portion remained [%]	96	83	81	108	104	107	98	95

^a The results are not corrected for the corresponding mean procedural recovery.

USE PATTERN

Meptyldinocap is a protectant and curative fungicide for the control of powdery mildew diseases in a range of crops. The product is diluted with water and applied as foliar spray or broadcast treatment using conventional spray equipment.

The registered uses in countries where supervised trials have been conducted or in countries with similar GAPs to where the supervised trials were carried out are summarised in Table 14.

Table 14 Registered uses of meptyldinocap 350 g/L EC formulation for foliar application

Crop	Country	Application			PHI days
		Rate, kg ai/ha	Spray conc. kg ai/hL	Max. No.	
Grapes, table and wine	Austria	0.042–0.21	0.021	4	21
Grapes, table	Chile	0.105–0.420	0.0105–0.021	4	45
Grapes, wine	Chile	0.105–0.420	0.0105–0.021	4	30
Grapes, table and wine	Croatia	0.175–0.21	0.0175–0.021	4	21
Grapes, table and wine	France	0.21	0.07–0.21	4	21
Grapes, table and wine	Greece	0.21	0.021–0.042	4	21
Grapes, table and wine	Hungary	0.21	0.021	4	21
Grapes, table and wine	Italy	0.028–0.21	0.014–0.021	4	21
Grapes, table and wine	Romania	0.14–0.21	0.014–0.021	4	21
Grapes, table and wine	Slovakia	0.175	0.0175–0.0583	4	21
Grapes, table and wine	Slovenia	0.175–0.21	0.0175–0.105	4	21
Grapes, table and wine	Tunisia	0.21	0.007	4	21
Grapes, table and wine	United Kingdom	0.21	0.021–0.084	4	21
Strawberries ^a	France	0.21	0.021–0.053	3	3
Strawberries ^a	Italy	0.056–0.21	0.014–0.021	3	3
Strawberries ^a	Slovenia	0.056–0.21	0.014–0.021	3	3
Strawberries ^b	United Kingdom	0.21	0.021–0.042	3	3

Crop	Country	Application			PHI days
		Rate, kg ai/ha	Spray conc. kg ai/hL	Max. No.	
Cucurbits ^{a,c}	France	0.21	0.021–0.105	3	3
Cucurbits ^{a,c}	Italy	0.056–0.21	0.014–0.021	3	3
Cucurbits ^{a,c}	Slovenia	0.056–0.21	0.014–0.021	3	3

^a outdoor and protected

^b protected

^c melons, watermelons, courgettes

RESIDUES RESULTING FROM SUPERVISED TRIALS

The Meeting received information on supervised field trials for meptyldinocap uses on cucumbers, courgettes, melons, grapes and strawberries.

Trial documentation included field and laboratory reports. Laboratory reports included procedural recoveries from spiking at residue levels similar to those occurring in the samples. Dates of analyses or duration of residue sample storage were also provided. Residue data are recorded unadjusted for recovery. The results of supervised trials are shown in Tables 15 to 18.

Following solvent extraction, the residues were hydrolysed to the corresponding phenols. Quantitation was performed using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). The validity of the results was confirmed with concurrent recovery tests performed in the same analytical batch. Concurrent recoveries from samples spiked at fortification levels of 0.025, to 1.0 mg/kg ranged from 72% to 110%. The LOD for the method was 0.01 mg/kg and the LOQ was 0.025 mg/kg. The analyses of samples were carried out within the period covered by the storage stability tests. The trials were performed in compliance with GLP and they were well documented.

Where multiple samples were taken from a single plot the highest value is reported. Where results from separate plots with distinguishing characteristics such as different formulations, varieties or treatment schedules were reported, results are listed for each plot. Results have not been corrected for concurrent method recoveries.

Cucumbers and courgettes

Table 15 Residues in cucumbers and courgettes treated with 353 g/L EC meptyldinocap formulation in glasshouses or plastic tunnels.

Crop Variety	Country Location Zone	No. of Appls	Appl. Rate (g ai/ha)	Appl. Conc. (g ai/hL)	PHI (days)	Portion Analysed	Meptyldinocap (mg/kg)	Trial ID DAS-Study ID
GAP in EU: maximum 3 applications at 10 days with maximum dosage of 0.21 kg ai/ha, PHI 3 days								
Courgettes Cora	France Pluneret NZ	3	194.4	34.96	< 0	Fruit	ND	F07W057R 2001017
			206.8	34.99	0	Fruit	0.09	
			212	34.98	3	Fruit	0.04	
					7	Fruit	< 0.005	
					14	Fruit	< 0.005	
Courgettes Leila	Germany Remseck NZ	3	203	35	< 0	Fruit	< 0.005	G07W088R 2001017
			198.6	26.24	0	Fruit	0.08	
			201.6	21	3	Fruit	0.02	
					7	Fruit	< 0.005	
					14	Fruit	< 0.005	
Courgettes Cora	France Thoree les Pins NZ	3	201.6	42	3	Fruit	< 0.005	F07W056R 2001017
			201.6	42				
			210	42				
Courgettes Diamant	Germany Hamburg	3	222.5	52.5	3	Fruit	0.02	G07W087R 2001017
			207.5	52.5				

Crop Variety	Country Location Zone	No. of Appls	Appl. Rate (g ai/ha)	Appl. Conc. (g ai/hL)	PHI (days)	Portion Analysed	Meptyldinocap (mg/kg)	Trial ID DAS-Study ID
	NZ		215	52.4				
Cucumber Tipo Espanol	Spain El Purrello SZ	3	210.7 213.3 198.1	20.94 20.93 20.94	< 0 0 3 7 14	Fruit Fruit Fruit Fruit	< 0.005 0.12 0.02 < 0.005 < 0.005	S07W018R 2001017
Cucumber Prestige	France Brouilla SZ	3	211.7 204.7 210	35 35 35	3	Fruit	0.01	F07W054R 2001017
Cucumber Tipo Espanol	Spain Canallas SZ	3	195.5 197.8 220.8	26.24 26.23 26.25	3	Fruit	< 0.005	S07W017R 2001017
Cucumber Noa	France Pernes les Fontaines SZ	3	200.3 218 209.6	21 21 21	< 0 0 3 7 14	Fruit Fruit Fruit Fruit Fruit	< 0.005 0.04 0.02 0.01 < 0.005	F07W055R 2001017

The applications were made 10 ± 1 days apart; < 0: samples taken before last application; < 0.005: residues were not detected above LOD; Validated LOQ: 0.025 mg/kg

Melons

Table 16 Meptyldinocap residues in melons treated with 353 g/L EC formulation in glasshouses.

Crop Variety	Country Zone Location	No. of Appls	Appl. Rate (g ai/ha)	Spray Vol (L/ha)	Appl. Conc. (g ai/hL)	PHI (days)	Portion Analysed	Meptyl dinocap (mg/kg)	Trial ID DAS- Study ID
GAP in EU: maximum 3 applications at 10 days with maximum dosage of 0.21 kg ai/ha, PHI 3 days									
Melon Anasta	France SZ	3	208 209 198	990 997 943	0.021 0.021 0.021	3	Peel Pulp Whole fruit	0.06 < 0.005 0.02	F07W058R DAS#2000673
Melon Anasta	France SZ	3	205 210 210	976 1000 1000	0.021 0.021 0.021	< 0 0 3 7 14	Whole Fruit	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005	S07W059R DAS#2000673
Melon Amigo	France NZ	3	204 190 206	388 362 393	0.021 0.021 0.021	3	Whole Fruit	0.008	F07W060R DAS 2000673
Melon Cantaloup	Spain SZ	3	219 216 217	835 821 826	0.021 0.021 0.021	3	Peel Pulp Whole fruit	0.16 < 0.005 0.05	S07W019R DAS#2000673
Melon Cantaloup	Spain SZ	3	211 224 215	803 853 818	0.021 0.021 0.021	< 0 0 3 7 14	Whole Fruit	< 0.005 0.06 0.02 < 0.005 < 0.005	S07W020R DAS#2000673
Melon Galia	Greece SZ Glasshouse	3	212 209 211	1009 997 1003	0.021 0.021 0.021	3	Whole Fruit	0.28 ^a	GR07W0153R DAS#2000673
Melon Delado	Germany NZ	3	209 213 209	597 810 993	0.021 0.021 0.021	< 0 0 3 7	Whole Fruit	< 0.005 0.01 0.02 0.01	G07W090R DAS 2000673

Crop Variety	Country Zone Location	No. of Appls	Appl. Rate (g ai/ha)	Spray Vol (L/ha)	Appl. Conc. (g ai/hL)	PHI (days)	Portion Analysed	Meptyl dinocap (mg/kg)	Trial ID DAS- Study ID
						14		< 0.005	
Melon Edgar	France SZ	3	207 222 204	394 422 389	0.021 0.021 0.021	< 0 0 3 7 14	Whole Fruit	< 0.005 0.05 0.02 < 0.005 < 0.005	F07W061R DAS2000673

The applications were made 10 ± 1 days apart; < 0: samples taken before last application; < 0.005: residues were not detected above LOD; Validated LOQ: 0.025 mg/kg.

^a Retained samples were re-analysed and the same residue level was found.

Grapes

A total of eighteen trials were conducted on grapes in Europe between 2005 and 2007. The first eight trials were done in 2005 (DAS 238405 and 238406) and have tested in side-by-side treatments two formulations: the first contained 350 g ai/L as a mixture of three 2,4-DNPOC and three 2,6-DNPOC isomers, and the second contained 350 g ai/ meptyldinocap a single 2,4-DNPOC isomer. In addition eight trials were conducted in 2006 with a formulation containing meptyldinocap (DAS 244659).

The last two trials were done in 2007 (DAS ref# 2000414) which was also used in the processing of grapes into wine. The 2,4-DNOP and 2,6-DNOP residues were detected separately and the residues were calculated back to the corresponding parent compound. Only the meptyldinocap concentration equivalents are reported in Table 17.

Table 17 Meptyldinocap residues in grapes treated four times with 350 g/L EC formulations.

Crop Variety	Country Zone	Appl. Rate (g ai/ha)	Spray Vol (L/ha)	PHI (days)	Portion Analysed	Residue ^a mg/kg	Trial ID Study ID Report No.
GAP in EU: maximum 4 applications at > 10 days with maximum dosage of 0.21 kg ai/ha, PHI 21 days							
Red wine grapes Grolleau	France NZ	200	679	< 0	Grapes	< 0.01	AF/8927/DE/1
		209	616	0	Grapes	0.15	AF_8927/DE/2
		213	732	7	Grapes	< 0.025	DAS# 238405
		209	734	14	Grapes	< 0.025	
				21	Grapes	< 0.025	
		28	Grapes	< 0.025			
Red wine grapes Pinot	France NZ	218	650	21	Grapes	< 0.025	AF/8927/DE/4
		229	683				DAS# 238405
		212	633				
		213	583				
White wine grapes Chenin	France NZ	211	611	21	Grapes	0.03	AF/8927/DE/2
		221	577				DAS# 238405
		210	688				
		197	633				
White wine grapes Chardonnay	France NZ	223	700	< 0	Grapes	< 0.01	AF/8927/DE/3
		208	672	0	Grapes	0.16	DAS# 238405
		209	741	7	Grapes	0.05	
		199	686	14	Grapes	0.03	
				21	Grapes	< 0.025	
				28	Grapes	< 0.025	
Red wine grapes Barbera	Italy SZ	231	1025	< 0	Grapes	< 0.01	AF/8928/DE/1
		207	965	0	Grapes	< 0.025	DAS# 238406
		208	980	7	Grapes	< 0.01	
		227	1060	14	Grapes	< 0.01	
				21	Grapes	< 0.01	
		28	Grapes	< 0.01			
Red wine grapes Garnacha	Spain SZ	218	1040	21	Grapes	< 0.025	AF/8928/DE/4
		210	999				AF_8928_DE
		221	1054				DAS# 238406

Meptyldinocap

Crop Variety	Country Zone	Appl. Rate (g ai/ha)	Spray Vol (L/ha)	PHI (days)	Portion Analysed	Residue ^a mg/kg	Trial ID Study ID Report No.
		207	985				
White wine grapes Montuni	Italy SZ	216 198 211 225	841 766 836 1023	21	Grapes	< 0.01	AF/8928/DE/2 AF_8928_DE DAS# 238406
White wine grapes Macabeo	Spain SZ	209 220 212 222	995 1048 1008 1059	0 7 14 21 28	Grapes Grapes Grapes Grapes	0.17 0.17 0.03 < 0.025 < 0.025	AF/8928/DE/3 AF_8928_DE DAS# 238406
Grape Gamay	Germany (NZ)	217 245 217 217	310 350 310 310	21	Grapes	0.03	AF/10346/DE/1 DAS#244659
White wine grapes Chardonnay	France NZ	212 200 188 208	1048 1004 1024 1040	< 0 0 7 14 21 28 35	Grapes Grapes Grapes Grapes Grapes Grapes Grapes	0.13 0.73 0.21 0.1 0.06 0.04 0.03	AF/10346/DE/2 DAS#244659
Grape Montuni	Italy (SZ)	212 224 199 205	1039 1000 1051 1058	21	Grapes	< 0.01	AF/10346/DE/3 DAS#244659
Grape Sangiovese	Italy (SZ)	214 230 208 215	1007 1139 1039 1107	< 0 0 7 14 21 28 35	Grapes Grapes Grapes Grapes Grapes Grapes Grapes	< 0.01 < 0.025 < 0.025 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	AF/10346/DE/4 DAS#244659
Grape Pinot noir	France NZ	203 218 198 188	1022 1022 992 1012	21	Grapes	< 0.01	AF/10346/DE/5 DAS#244659
Grape Riesling	Germany (NZ)	192 216 184 216	946 978 978 929	21	Grapes	0.12	AF/10346/DE/6 DAS#244659
Grape Spatburgunder	Germany (NZ)	209 208 205 213	995 991 978 1013	21	Grapes	< 0.025	AF/10346/DE/7 DAS#244659
Grape Kerner	Germany (NZ)	212 208 205 200	1008 991 975 954	19	Grapes	0.08	AF/10346/DE/8 DAS#244659
Table grapes Crimson seedless (red)	Greece (SZ)	208 210 211 202	991 999 1003 960	21	Grapes Raisins	0.03 0.065	GR07W010R DAS# 2000414
Table grapes Thomson seedless (white)	Greece (SZ)	210 210 208 211	1002 1000 992 1003	21	Grapes Raisins	0.06 < 0.025	GR07W011R DAS# 2000414

^a meptyldinocap residue measured after hydrolysis as the sum of parent and its phenol derivative;

NZ, SZ: North and South zones for trials in European Union, respectively; < 0: samples taken before last application; < 0.01: residues were not detected above LOD; Validated LOQ: 0.025 mg/kg.

Strawberries

Table 18 Meptyldinocap residues in strawberries treated three times with 353 g/L EC formulations in glasshouse

Crop Variety	Country Zone Location	Appl Rate (g ai/ha)	Spray Vol (L/ha)	PHI (days)	Portion Analysed	Meptyl dinocap (mg/kg)	Trial ID DAS- Study ID
GAP in EU: maximum 3 applications at 10 days with maximum dosage of 0.21 kg ai/ha, PHI 3 days							
Strawberry Pajaro	France	213	608	3	Fruit	0.05	F07W050R DAS#2000312
	SZ	230	659		Unwashed	0.07	
	Glasshouse	222	935		Jam Canned	ND 0.05	
Strawberry Pajaro	France	223	983	< 0	Fruit	ND	S07W051R DAS#2000312
	SZ	210	1001	0		0.23	
	Glasshouse	220	1049	3		0.09	
				7		0.02	
			14	ND			
Strawberry Pajaro	Spain	206	976	< 0	Fruit	ND	S07W015R DAS#2000312
	SZ	210	1000	0		0.47	
	Glasshouse	210	1000	3		0.03	
				7		0.03	
			14	ND			
Strawberry Pajaro	Spain	200	954	3	Fruit	0.08	S07W016R DAS#2000312
	SZ	210	1000				
	Glasshouse	209	995				
Strawberry Elsanta	Germany	206	1960	3	Fruit	0.11	G07W036R DAS#2000312
	NZ	205	1948		Unwashed	0.13	
	Glasshouse	207	1975		Jam Canned	0.06 0.11	
Strawberry Cerafine	France	213	507	3	Fruit	0.06	F07W052R DAS 2000312
	NZ	214	510				
	Glasshouse	226	538				
Strawberry Mara DesBois	France	210	500	< 0	Fruit	0.11	F07W053R DAS 2000312
	NZ	190	452	0		0.14	
	Glasshouse	211	503	3		0.11	
				7		0.06	
			14	0.03			
Strawberry Elsanta	UK	203	207	< 0	Fruit	0.11	FGB7W015R DAS2000312
	NZ	200	203	0		0.20	
	Glasshouse	203	207	3		0.12	
				7		0.03	
			14	ND			

< 0: samples taken before last application; ND: residues were not detected (LOD: 0.01 mg/kg) Validated LOQ: 0.025 mg/kg.

FATE OF RESIDUES IN STORAGE AND PROCESSING*In processing**Grapes*

Mature grape bunches were collected from vineyards maintained according to good agriculture practices. Dinocap was applied 6–8 times during the growing season at recommended or about 1.5× maximum rate. Part of the collected bunches were subject to vinification processes similar to commercial practices.

The grapes of the white variety were crushed and the juice was separated from the skins, seeds and stems by pressing immediately afterwards. The must was divided into two equal portions. One was processed further without heating; the other was pasteurized for 2 minutes at approximately

85 °C. After cooling, the pasteurized portion was processed further in the same way as the unheated portion.

The crushed and destemmed red grapes were heated to 60 °C prior to the pressing in order to simulate pre-fermentation heat treatment. After cooling, the juice was separated by pressing.

The must of the white wine grapes both pasteurized and non pasteurized, as well as the must of the red wine grapes was processed into wine following the same processing steps:

- fermentation
- clarification (first racking and second racking)
- filtration, bottling and maturation.

The samples from processed products were taken as:

- must—after juice separation (pressing)
- young wine—after ageing in a glass carboy for 8–10 weeks
- mature wine—storage after bottling for 5–6 months.

The samples were sent to the analytical laboratory deep-frozen and stored there until analyses.

The residues were determined as total dinocap with GC-ECD following hydrolysis and methylation. The LOQ of the method was 0.04 mg/kg (DAS#247240, DAS#246642 and DAS#110298) and 0.05 mg/kg (DAS#145276 and DAS#110298). Average recoveries in grapes, must and wine were within the acceptable 70–120% range. All samples had been analysed within the 23 month period covered by the storage stability tests. Part of the trials listed below had been reported by the 1998 JMPR. They are listed for completeness.

Table 19 Total dinocap residues in grapes and processed products following multiple applications of dinocap EC formulations

Crop Variety	Country Zone	No. of Appls	Appl Rate ^a (g ai/ha)	Appl Conc (g ai/hL)	PHI (days)	Portion Analysed	Total Dinocap mg/kg	Trial ID Study ID Report No. Trial Year
Red wine grapes Pinot Nero	Italy SZ	6	193	17.5	0	Grapes	0.27 ^a	4049263 ER64_12 1992 DAS#247240
			209	17.5	20	Grapes	< 0.04	
			175	17.5				
			173	17.5				
Red wine grapes Barbera	Italy SZ	6	314	17.5	0	Grapes	0.262 ^a	4049262 ER64_12 1992 DAS#247240
			298	17.5	20	Grapes	< 0.04	
			277	17.5	20	Must	< 0.04	
			276	17.5	20	Must, Flow	< 0.04	
					20	Must, Half-ferm.	< 0.04	
			20	Pomace, wet	< 0.04			
20	Wine	< 0.04						
Red wine grapes Merlot Noir	France SZ	6	210	–	14	Bunch	0.10	4219246 ER66_19 1992 DAS#246642
			210	–	14	Must	< 0.04	
			210	–	14	Wine	< 0.04	
			210	–				
Red wine grapes Pinot Nero	Italy SZ	6	222.13	21.9	0	Grapes	0.30	4839302 ER R67_9/ER R67_10 1993 DAS#247243
			230.6	21.9	20	Grapes	< 0.04	
			232.71	21.9	20	Must	< 0.04	
			258.1	21.9	20	Must, Flow	< 0.04	
					20	Pomace, wet	< 0.04	
20	Wine	< 0.04						

Crop Variety	Country Zone	No. of Appls	Appl Rate ^a (g ai/ha)	Appl Conc (g ai/hL)	PHI (days)	Portion Analysed	Total Dinocap mg/kg	Trial ID Study ID Report No. Trial Year
Red wine grapes Pinot Nero	Italy SZ	6	182.57 237.3 235.32 243.43	21 21 21 21	0 20 20 20 20 20	Grapes Grapes Must Must, Flow Pomace, wet Wine	0.3365 ^a < 0.04 < 0.04 < 0.04 < 0.04 < 0.04	4839302 ER R67_9/ER R67_10 1993 DAS#247243
Red wine grapes Barbera	Italy SZ	6	312.97 297.33 305.15 328.62	21.9 21.9 21.9 21.9	0 20 20 20 20 20	Grapes Grapes Must Must, Flow Pomace, wet Wine	0.545 ^a < 0.04 < 0.04 < 0.04 < 0.04 < 0.04	4839301 ER R67_9/ER R67_10 1993 DAS#247243
Red wine grapes Barbera	Italy SZ	6	322.47 284.97 292.47 299.97	21 21 21 21	0 20 20 20 20 20	Grapes Grapes Must Must, Flow Pomace, wet Wine	0.647 < 0.04 < 0.04 < 0.04 < 0.04 < 0.04	4839301 ER R67_9/ER R67_10 1993 DAS#247243
Red wine grapes Fruhburgunder	Germany NZ	8	302 319 338 342	21 21 21 21	0 7 14 21 28	Grapes Grapes Grapes Grapes Grapes	1.72 0.617 0.495 0.363 0.223	RAS17_2G RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
Red wine grapes Fruhburgunder	Germany NZ	8	293 317 332 336	21 21 21 21	0 7 14 21 28	Grapes Grapes Grapes Grapes Grapes	1.74 0.498 0.417 0.223 0.144	RAS17_2G RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
Red wine grapes Spatburgunder	France NZ	8	294 318 341 333	21 21 21 21	0 7 14 21 28	Grapes Grapes Grapes Grapes Grapes	2.02 1.18 0.772 0.499 0.443	RAS17_2F RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
Red wine grapes Spatburgunder	France NZ	8	289 318 341 341	21 21 21 21	0 7 14 21 28	Grapes Grapes Grapes Grapes Grapes	2.06 0.924 0.673 0.419 0.325	RAS17_2F RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
Red wine grapes Spatburgunder	France NZ	8	291 316 331 337	21 21 21 21	0 7 14 21 28	Grapes Grapes Grapes Grapes Grapes	0.968 0.645 0.578 0.218 0.431	RAS17_4F RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
Red wine grapes Spatburgunder	France NZ	8	291 314 333 337	21 21 21 21	0 7 14 21 28 21 21	Grapes Grapes Grapes Grapes Grapes Juice (must) Mature wine Young Wine	1.5 0.796 0.470 0.592 0.432 < 0.05 ND ND	RAS17_4F RAS 17/980214 ER 72.1 & ER 72.2 Y 1997 DAS#145276
White wine grapes Kerner	Germany NZ	8	295 317 335 339	21 21 21 21	0 7 14 21 28	Grapes Grapes Grapes Grapes Grapes	1.305 0.791 0.364 0.261 0.191	RAS17_1G RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
White wine grapes Kerner	Germany NZ	8	300 315 342 334	21 21 21 21	0 7 14 21 28	Grapes Grapes Grapes Grapes Grapes	0.679 0.696 0.323 ND 0.181	RAS17_1G RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
White wine	France	8	171	21	0	Grapes	0.928	RAS17_1F

Crop Variety	Country Zone	No. of Appls	Appl Rate ^a (g ai/ha)	Appl Conc (g ai/hL)	PHI (days)	Portion Analysed	Total Dinocap mg/kg	Trial ID Study ID Report No. Trial Year
grapes Silvaner	NZ		194 215 213	21 21 21	7 14 21 28	Grapes Grapes Grapes Grapes	0.487 0.228 0.221 0.266	RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
White wine grapes Silvaner	France NZ	8	173 187 215 210	21 21 21 21	0 7 14 21 28	Grapes Grapes Grapes Grapes Grapes	0.939 0.337 0.311 0.146 0.225	RAS17_1F RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
White wine grapes Muller-Thurgau	France NZ	8	165 192 213 210	21 21 21 21	0 7 14 21 28	Grapes Grapes Grapes Grapes Grapes	1.11 0.725 0.391 0.280 0.278	RAS17_3F RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
White wine grapes Muller-Thurgau	France NZ	8	170 191 208 215	21 21 21 21	0 7 14 21 28 21 21 21	Grapes Grapes Grapes Grapes Grapes Juice (must) Mature wine Young Wine	1.22 0.588 0.349 0.348 0.2253 < 0.05 ND ND	RAS17_3F RAS 17/980214 ER 72.1 & ER 72.2 1997 DAS#145276
Red Wine Grapes Barbera	Italy	5	175 175 175 175	— — — —	0 20 40 60	Grapes Grapes Grapes Grapes	0.288 ^b < 0.05 ^b < 0.05 ^b < 0.05 ^b	4049141 R62.6 1992 DAS#260127
Red Wine Grapes Barbera	Italy SZ	6	140 140 175 175	— — — —	0 20 20 20	Grapes Grapes Grapes Grapes	0.285 ^b < 0.05 ^b < 0.05 ^b < 0.05 ^b	4049140 R62.6 1992 DAS#260127
White Wine Grapes Cortese	Italy SZ	7	175 175 175 175	— — — —	0 32 32 32	Grapes Grapes Must Wine	0.200 ^b < 0.05 ^b < 0.05 ^b < 0.05 ^b	4049150 R62.6 1992 DAS#260127
White Wine Grapes Garganega	Italy SZ	5	175 175 175 157.5	— — — —	0 20	Grapes Grapes	1.093 ^b 0.3 ^b	4049142 R62.6 1992 DAS#260127
White Wine Grapes	Italy SZ	5	175 175 175 157.5	— — — —	20	Grapes	0.304 ^b	4049142 R62.6 1992 DAS#260127
Red wine grapes Portugieser	Germany NZ	8	291 303 332 333	— — — —	0 7 14 21 28 21 21 21	Grapes Grapes Grapes Grapes Grapes Juice Mature wine Young Wine	1.3 0.82 0.55 0.33 0.46 < 0.05 ND ND	R&H/204/3/G R&H 204/973651 1996 DAS#110298
White wine grapes Muller-Thurgau	Germany NZ	8	288 316 352 337	— — — —	0 7 14 21 28 21 21 21	Grapes Grapes Grapes Grapes Grapes Juice Mature wine Young Wine	1.76 1.03 0.74 0.67 0.46 < 0.05 ND ND	R&H/204/2/G R&H 204/973651 1996 DAS#110298
White wine grapes Riesling	Germany NZ	8	330 372 421	— — —	0 7 14	Grapes Grapes Grapes	1.97 1.52 0.64	R&H/204/1/G R&H 204/973651 1996

Crop Variety	Country Zone	No. of Appls	Appl Rate ^a (g ai/ha)	Appl Conc (g ai/hL)	PHI (days)	Portion Analysed	Total Dinocap mg/kg	Trial ID Study ID Report No. Trial Year
			410	—	21 28	Grapes Grapes	0.66 0.42	DAS#110298
Table grapes Crimson seedless (red)	Greece (SZ)	4	208 210 211 202		21	Grapes Raisins	0.03 0.065 ^c	GR07W010R DAS# 2000414
Table grapes Thomson seedless (white)	Greece (SZ)	4	210 210 208 211		21	Grapes Raisins	0.06 < 0.025	GR07W011R DAS# 2000414

^a data for the last 4 treatments are listed; all applications were made 15–20 days apart.

^b reported as DNOPC; ND: residues were below the limit of detection (LOD) of 0.01 mg/kg.

^c mean of 0.1 mg/kg (first analysis) and 0.03 mg/kg in the retained sample (replicate analyses from the same sample)

Strawberries

Four trials were reported which included residues in strawberry jams and preserves. Two trials performed with max GAP are also summarised in Table 19. Two additional trials were conducted at 0.32–0.44 kg ai/ha dosage rate (approximately 1.5× and 2×) applied six times. The fruits were harvested 3 days after last applications and processed.

These samples were immediately frozen in the field at approximately –20 °C and transferred deep-frozen to the testing laboratory. Sampling to analysis intervals ranged from 319 to 362 days.

Preparation of jam

The washed strawberries, sugar and water were placed in a steam pan and heated until the sugar dissolved. The beating time and final temperature was recorded. The pectin was mixed to a smooth consistency in water at approximately 80 °C and added to the fruit mix. The mixture was boiled until the soluble solids reached approximately 63 ° Brix. The concentration time was recorded. The citric acid was then added. The jam was hot filled into pre rinsed 1 lb glass jars using a fill weight of 415 g ± 1 g. The jars were manually capped using RTO pickle finish closures, inverted and left to cool.

Preparation of Pasteurised strawberries in water

The strawberries were sorted and any foreign material or rotten strawberries were removed. The calyx was removed and the strawberries were washed under a spray of potable mains water and allowed to drain for at least two minutes. The weight of washed strawberries was recorded. The strawberries were filled into pre rinsed 1 lb glass jars using a fill weight of 215 g ± 1 g. Water (at approximately 92 °C) was added to a fill weight of 115 g ± 1 g. The jars were steam flow closed using RTO pickle finish closures. The jars were pasteurised in a tank of water at an initial temperature of 55–60 °C. The water temperature was increased to 90 °C and the jars were maintained at process temperature until a P value of 10 was achieved. After processing all samples were transferred to a frozen storage area operating at below –18 °C. The residues were determined as DNOP with LOQ of 0.025 mg/kg, LOD of 0.01 mg/kg and average recovery of 108%.

Table 20 Total dinocap residues in strawberry and processed products following multiple applications of dinocap EC formulations

Crop Variety	Country Zone Location	No. of Appls	Appl Rate ^a (g ai/ha)	PHI (days)	Portion Analysed	Total dinocap mg/kg	Trial ID Study ID Report No. Trial Year
Strawberry Elsanta	United Kingdom NZ ^b	6	407	0	Berries	0.50	AK/3280/HL/1UK R&H 230/973653 R 69.5 1996 DAS#219899
			414	3	Berries	0.23	
			406	3	Jam	0.079	
			401	3	Preserve	< 0.05	
Strawberry Elsanta	United Kingdom NZ ^b	6	382	0	Berries	0.74	AK/3280/HL/2UK R&H 230/973653 R 69.5 1996 DAS#219899DAS#219899
			387	3	Berries	0.31	
			415	3	Jam	0.070	
			442	3	Preserve	0.11	
Strawberry Pajaro	France SZ ^c	3	213	3	Canned	0.05	F07W050R 20074012/E1-FGST GHE-P-11833 2007 DAS#2000312
			223	3	Fruit, whole	0.05	
			222	3	Jam	ND	
				3	Unwashed fruit	0.07	
Strawberry Elsanta	Germany NZ ^c	3	206	3	Canned	0.11	G07W036R 20074012/E1-FGST GHE-P-11833 2007 DAS#2000312
			204	3	Fruit, whole	0.11	
			207	3	Jam	0.06	
				3	Unwashed fruit	0.13	

^a data for the last 4 treatments are listed

^b Outdoor

^c Glasshouse or plastic tunnel

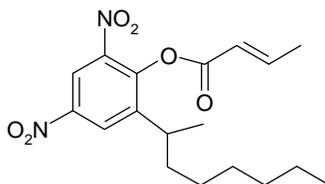
RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

No feeding study was provided as none of the raw agricultural commodities are animal feed items.

APPRAISAL

Meptyldinocap is a protectant and curative fungicide for the control of powdery mildew diseases. As a new compound it is evaluated at the first time by the JMPR. The meptyldinocap is the single isomer [2,4-dinitro-6-(1-methylheptyl)phenyl crotonate] of the existing active substance dinocap.



The 2,4-dinitro-6-(1-ethylhexyl)phenyl crotonate, present in the technical meptyldinocap in 1.5% concentration, is considered an impurity. The dinocap is a mixture of 2,4-dinitro-6-octylphenyl crotonates and 2,6-dinitro-4-octylphenyl crotonates. The 'octyl' being a mixture of 1-methylheptyl, 1-ethylhexyl and 1-propylpentyl groups. Approximately 22% of dinocap is meptyldinocap. Dinocap was last evaluated as new compound by the 1998 (R) and for some additional commodities by the 2001

Meetings of the JMPR. Presently both dinocap and meptyldinocap are marketed, but the manufacturers intend to gradually replace dinocap with meptyldinocap.

The manufacturer submitted information on metabolism in plants, analytical methods and residues in/on pome fruits, stone fruits, grapes, strawberries, cucurbits with edible and inedible peel which were evaluated by the present Meeting.

The studies evaluated by the present Meeting were conducted either with meptyldinocap or dinocap. The typical composition of the test substances are given below:

Isomers	Meptyldinocap	Dinocap
Meptyldinocap, 2,4-dinitro-6-(1-methylheptyl)phenyl crotonate	98.5%	22%
2,6-dinitro-4-(1-methylheptyl)phenyl crotonate	0%	11%
2,4-dinitro-6-(1-ethylhexyl)phenyl crotonate ¹	1.5%	22%
2,6-dinitro-4-(1-ethylhexyl)phenyl crotonate	0%	11%
2,4-dinitro-6-(1-propylpentyl)phenyl crotonate	0%	22%
2,6-dinitro-4-(1-propylpentyl)phenyl crotonate	0%	11%

Animal metabolism

The intended use for meptyldinocap is on vines, cucurbits and strawberries, which are not fed to animals. Therefore, no animal metabolism studies were provided for evaluation.

Farm animal metabolism studies evaluated by previous Meetings of the JMPR indicated that no radioactive residues were detectable in milk or tissues when lactating caws were fed with dinocap at 0.1, 0.3 and 1 ppm dose levels.

Plant metabolism

The plant metabolism studies on apples, cucumbers and squash submitted to the current meeting had already been evaluated by the 1998 JMPR, and were re-evaluated by the present Meeting. The metabolism studies were carried out with meptyldinocap. A single major metabolite [2, 4-dinitro-6-(1-methylheptyl) phenol] was identified and it is referred to as 2,4-DNOP.

An apple tree was treated with a single foliar application of an EC formulation containing 45.6% ai at a rate equivalent to 1.96 kg ai/ha, four times the normal maximum application rate (0.49 kg ai/ha). Apple and leaf samples were taken on the day of application, both before and after treatment, and after 7, 14, and 21 days. Half of each fruit sample was analysed as whole fruit, and the other half peeled and the peel and pulp analysed separately.

The samples were extracted with methanol which recovered more than 90% of the radioactivity from the day 0 samples and 40–60% from the aged samples. More than 92% of the radioactivity at each PHI was associated with the peel. The total radioactivity recovered in the neutral and alkaline methanolic extracts was more than 80% in all cases.

Two compounds present in the apple fruit have been identified by co-elution with standards in both normal phase TLC and reversed phase HPLC. These are the parent meptyldinocap and its corresponding phenol, 2,4-DNOP. The parent compound was present in all of the treated samples. On the day of treatment, meptyldinocap was present at 2.12 mg/kg. After seven days the level had fallen to 0.52 mg/kg, representing 23% of the total radioactivity. After 14 days, the concentration of

meptyldinocap had decreased to 0.25 mg/kg (11% of the total radioactivity), and after 21 days it was present at 0.12 mg/kg (8% of the total radioactivity). The half-life of meptyldinocap was calculated to be 5.2 days. The single major metabolite, 2,4-DNOP, was present at lower levels: it comprised of roughly 24% of the total radioactivity in the aged samples (0.03–0.08 mg/kg, expressed as parent equivalent).

Five minor metabolites could be identified by gas chromatography with mass spectrometric detection: [2-methyl-5-nitro-7-(2-octyl) benzoxazole, 2-(hydroxymethyl)-5-nitro-7-(2-octyl) benzoxazole, 4-(1-propenyl)-5-nitro-7-(2-octyl)benzoxazole, 5-nitro-7-(octyl) benzoxazole and 2-hydroxymethyl-5-nitro-(2-octyl)-phenyl crotonamide]. The corresponding concentrations ranged from 0.001–0.007 mg/kg.

In cucumbers, the distribution and rate of decrease of residues after a single treatment with ^{14}C -meptyldinocap at 0.56 kg ai/ha were studied. The residues of ^{14}C -meptyldinocap dissipated rapidly from the cucumber leaves and stems. The half lives of radioactive residues on leaves and stems were 11.8 days and 18.8 days, respectively. The ^{14}C residues on the leaves decreased from 38.2 mg/kg immediately after application to 1.4 mg/kg at final harvest. The ^{14}C residues in the stems decreased from 3.6 mg/kg immediately after application to 0.5 mg/kg at final harvest, 65 days after last application.

The whole mature fruit harvested 48 days after application contained ^{14}C residues of 0.16 mg/kg and whole mature fruit harvested 63 days after application contained 0.09 mg/kg. Of the whole mature fruit harvested 48 days after application, the peels contained 0.15 mg/kg and the flesh contained 0.11 mg/kg. The proportion of parent compound and 2, 4-DNOP was about the same in cucumber fruits at days 48 and 63.

Of the residues extracted from the leaves by acetone, only one metabolite (2,4-DNOP) occurred in significant (> 10%) quantity. The metabolism of ^{14}C -meptyldinocap in cucumber leaves was extensive, leading to 18 minor metabolites. Only 2,4-DNOP could be identified amounting to 2.4% of TRR at day 8, while the unextractable residues accounted for 58% of TRR.

The half-life of the radioactivity was 8 days in the squash leaves treated with ^{14}C -meptyldinocap at two times the rate of 0.56 kg ai/ha. 2,4-DNOP was the main metabolite in the leaves and was also found in the fruit. About six unidentified metabolites were found in the fruit and 10 in the leaves, none of which individually accounted for more than 10% of the TRR. The 2,4-DNOP, meptyldinocap, organic-soluble metabolites and water-soluble polar metabolites and unextractable ^{14}C -residues amounted to 1.3%, 5.9%, 5.5%, 21% and 57.6% of TRR, respectively.

Photolysis, under natural daylight conditions, played a major role in the rapid dissipation of meptyldinocap from plant foliage. The concentration of meptyldinocap did not change on covered leaves over 27 hours following the foliar treatment with ^{14}C -meptyldinocap, while it decreased to 39% on leaves exposed to natural light. The extract of 27-hour uncovered leaves contained 53% polar photoproducts.

In summary, the metabolism of meptyldinocap is complex, resulting in a large number of metabolites present at low concentrations. The metabolism of 2, 4-meptyldinocap appears to proceed by relatively rapid hydrolysis of the crotonate ester (half lives are about 5, 8 and 11.8 days on apple fruits, squash and cucumber leaves, respectively) to the corresponding phenol (2,4-DNOP). The phenol is then further metabolised rapidly to a large number of more polar compounds, none of which is present in a significant amount. The proposed pathway for the formation of minor metabolites involves reduction of a nitro group to the amine. Metabolites are then formed by reaction of the amine with formic or acetic acid to form amides, or by intramolecular transfer of the crotonyl group to form the crotonamide. Ring closure of the amides then forms benzoxazoles. Individual metabolites could not be isolated. The amines could readily form conjugates with acids to form amides. Further degradation led to small carbon units which were subsequently incorporated into a number of natural products including cutin, lignin and other constituents that make up the acid detergent fibre.

Environmental fate in soil

Soil metabolism, degradation, leaching and rotational crop studies are not required for compounds with intended use of foliar applications only on permanent crops with no crops planted in rotation.

As part of the plant metabolism studies soil samples were also taken and analysed for meptyldinocap residues.

The ^{14}C residues in the top 2.5 cm of soil from the cucumber plot decreased from 0.45 mg/kg immediately after application to 0.31 mg/kg after 63 days. The ^{14}C residues in the 2.5–7.6 cm soil depth never exceeded 0.02 mg/kg and the 7.6–15.2 cm soil depth residues never exceeded 0.007 mg/kg.

The ^{14}C residues in the top section of the soil (0–2.5 cm) of the squash plot decreased from 0.43 mg/kg after the last treatment to 0.40 mg/kg 63 days later. The ^{14}C residues in the other soil sections were low.

The residues of [^{14}C]meptyldinocap in the soil in which the cucumber or squash were grown dissipated at a much slower rate than from the plants. There appeared to be no significant leaching of [^{14}C]-meptyldinocap residues into the lower depths of the soil.

Metabolism in Rotational Crops

The studies evaluated by the 1998 JMPR indicated that when beans, oats and turnips were grown in soil in which cucumber and squash were treated with [^{14}C]meptyldinocap 250 days earlier, the radioactive residues in samples taken until maturity of crops were at or below 0.02 mg/kg. Consequently, residues in follow up crops are unlikely to occur in measurable concentration.

Methods of analysis

The analytical methods used for determination of meptyldinocap residues in supervised trials were principally the same as those evaluated by the 1998 JMPR. Following the solvent extraction, the residues were converted to the corresponding phenols and determined by GC after methylation or analysed directly by HPLC-MS/MS. The validated limit of quantification for the meptyldinocap was 0.025 mg/kg and for combined residues 0.05 mg/kg. The average recoveries ranged from 80 to 104% with relative standard deviation of 7–14%. The concurrent recoveries obtained during the analysis of samples were in the same range.

The DFG S-19 multi residue method was found to be suitable for the determination of meptyldinocap residues in apples, barley grain, grapes and soya bean flour in the concentration range of 0.05 mg/kg to 1.0 mg/kg with a validated limit of quantitation (LOQ) of 0.025 mg/kg for the parent compound. The meptyldinocap peak was well separated from the dinocap isomers under the gas chromatographic conditions applied. The independent laboratory validation trials were conducted to satisfy the relevant requirements of the European Commission and the U.S. EPA Guidelines.

Stability of residues in stored analytical samples

The stability of residues were tested in apples and grapes using 97.5% pure 2,4-dinitro-6-octylphenyl crotonates (2,4-DNOPC isomers) and 2,6-dinitro-4-octylphenyl crotonate isomer mixtures. The 'octyl' being a mixture of 1-methylheptyl, 1-ethylhexyl and 1-propylpentyl groups, in a separate set of experiments. The untreated samples were spiked at 1 mg/kg level. The overall mean procedural recoveries for 2,4-dinitro-6-octylphenyl crotonates in grapes and apples were 94.5% (RSD: 5.25%) and 88.6% (RSD: 10.3%). The average of residues that remained over the period of 24 months were 89.8% (RSD: 10.13%) and 71.5% (RSD: 10.5%), respectively. The results indicate that residues of the 2,4-DNOPC isomers are stable in apples, grapes, tomatoes, peaches and strawberries stored frozen up to 24 months. The stability of the meptyldinocap alone during deep-frozen storage could not be determined from these studies. However, it may be assumed to be similar to the other isomers.

Definition of the residue

Results of metabolism studies on fruits and fruiting vegetables indicate that the parent compound, meptyldinocap, forms the main residue remaining in the plant tissues at harvest. The major metabolite, (the corresponding phenol, 2,4-DNOP), showed concentrations of 2–10% of total radioactivity only. The concentration of the major metabolite, (the corresponding phenol 2, 4-DNOP) had not changed with time after applications of the pesticide, indicating that further metabolism to a number of minor compounds occurred relatively quickly. Initially the meptyldinocap amounted to the major portion of the TRR. The proportion of 2, 4-DNOP gradually increased with time and it was present in about the same concentrations as meptyldinocap, 48–63 days after the treatment of cucumber. The parent/2, 4-DNOP ratio was about 4 in apples, 21 days after application.

The analytical method, which is used in the residue trials, determined meptyldinocap residues as a sum of the parent and the corresponding phenol. Multi residue methods, based on gas chromatographic and HPLC-MS/MS detection are available for the determination of meptyldinocap alone and have been validated for four representative commodities. Residues deriving from the use of dinocap could be identified based on the presence of 2,6-DNOP isomers provided that the chromatographic system used has sufficient resolution.

The current residue definition of dinocap is dinocap. As meptyldinocap is one isomer of dinocap, it is covered by the current residue definition. Non-selective methods cannot distinguish meptyldinocap from dinocap, but selective methods are available. While meptyldinocap and dinocap are both registered for crop uses, it is preferable, for enforcement purposes, to maintain a single residue definition.

It follows that, at least while dinocap MRLs are maintained, the residue definition for meptyldinocap as "dinocap, sum of all isomers" would be a practical solution.

The present Meeting established an ADI of 0–0.02 mg/kg/bw day. The new ADI is applicable for the sum of meptyldinocap and its corresponding phenol, when only they are present in the commodities analysed.

The Meeting recommended that while dinocap MRLs are maintained, the residue definition for meptyldinocap enforcement purposes should be dinocap, sum of all isomers.

Definition of the residue for dietary exposure assessment: the sum of meptyldinocap and the corresponding phenol, 2,4-DNOP, expressed as the parent meptyldinocap.

A residue definition for animal products is not required as no residue is expected to occur in animal products from the targeted use of meptyldinocap.

Results of supervised trials on crops

All trials were conducted according to GAP and the samples were analysed within the tested deep-frozen storage period. The methods applied for the analyses of samples determine meptyldinocap residues as a sum of the parent and the corresponding phenol. The validity of the results was confirmed with concurrent recovery tests performed in the same analytical batch.

Cucumber and courgettes

GAP in France, Italy and Slovenia permits a maximum of three applications at 10 days with maximum dosage of 0.21 kg ai/ha and a PHI of 3 days. A total of eight supervised field trials on cucumbers/courgettes were conducted according to maximum GAP in greenhouses located in the North and South European zones. Samples collected 3 days after the last application contained residues of < 0.005 (2), 0.01, 0.02 (4) and 0.04 mg/kg.

The Meeting estimated a maximum residue level, STMR value and HP value for fruiting vegetables, cucurbits, except melons of 0.07, 0.02 and 0.04 mg/kg.

Melons

GAP in France, Italy and Slovenia permits a maximum of three applications at 10 days with a maximum rate of 0.21 kg ai/ha and PHI of 3 days. A total of eight supervised field trials on melons were conducted according to maximum GAP in the North and South European zones. Whole fruit samples collected 3 days after the last application contained residues: < 0.005, 0.008, 0.02 (4), 0.05 and 0.28 mg/kg. No detectable residues were found in pulp samples.

The Meeting estimated a maximum residue level, STMR value and HP value for melons of 0.5, 0.005 and 0.28 mg/kg, respectively. Note: there is no information on pulp residues at high whole fruit residue.

The Meeting recommended to re-evaluate the current CXL of 0.05* for dinocap in fruiting vegetables cucurbits.

Grapes

GAP in France, Greece, Hungary and the UK permits a maximum of four applications with a maximum rate of 0.21 kg ai/ha and a PHI of 21 days. A total of eighteen trials were conducted on grapes in Europe between 2005 and 2007. Eight trials with two formulations side by side containing meptyldinocap alone and the mixture of 2,4-DNPOC and 2,6-DOPOC (three isomers of each compound). In addition, eight trials were conducted in 2006 with a formulation containing meptyldinocap. All trials were performed with the permitted maximum application rate and frequency.

Samples collected at day 21 following the last application of meptyldinocap contained residues: < 0.01 (5), < 0.025 (6), 0.03 (3), 0.06 (2), 0.08, and 0.12 mg/kg.

The Meeting estimated a maximum residue level, STMR value and HP value for grapes 0.2, 0.025 and 0.12 mg/kg, respectively.

The Meeting noted that the current CXL of 0.5 mg/kg for dinocap in grapes covers the residues deriving from the use of meptyldinocap.

Strawberries

The GAP of France, Italy and Slovenia permits a maximum of three applications at 10 day intervals with a maximum rate of 0.21 kg ai/ha and a PHI of 3 days. A total of eight supervised field trials on strawberries were conducted according to the maximum GAP in greenhouses located in Northern and Southern Europe. The pesticide treatment was made with a formulation containing meptyldinocap.

Residues in samples collected 3 days after the final application of meptyldinocap, in ranked order, were: 0.03, 0.06, 0.07, 0.08, 0.09, 0.11, 0.12 and 0.13 mg/kg.

The Meeting estimated a maximum residue level, STMR value and HP value for grapes 0.3, 0.085 and 0.13 mg/kg, respectively

The Meeting noted that the current CXL of 0.5 mg/kg for dinocap in strawberries covers the residues derived from the use of meptyldinocap.

The Meeting also noted that the current CXL for dinocap in strawberries included a note that it excludes the glasshouse use. The recommended maximum residue level for meptyldinocap is applicable for both uses.

Fate of residues during processing

Grapes

Dinocap was applied 6–8 times to both red and white grape varieties during the growing season at the recommended or 1.5× rate. Samples were collected for processing at intervals of 14–21 days after the final application. A portion of the collected grape bunches were subjected to vinification similar to commercial practice. The must from the white grape was divided into two equal portions; one of

which was processed further without heating, the other was pasteurized for 2 minutes at approximately 85 °C.

The must of the white wine grapes, both pasteurized and non pasteurized, as well as the must of the red wine grapes was processed into wine following the same processing steps: fermentation; clarification (first racking and second racking); filtration, bottling and maturation. The residues were analysed with methods having LOQs of 0.04 and 0.05 mg/kg and an LOD of 0.01 mg/kg. The average recoveries in grapes, must and wine were in the 70–120% range.

Six grape samples taken 20–21 days or at shorter intervals after the last treatment did not contain residues above the LOQ. These trials could not be used for estimation of the processing factor. Other trials on red and white grapes resulted in measurable residues in grapes harvested 14–21 days after last pesticide treatment. The results of processing studies are summarised below:

PHI (days)	14	21	21	21 ^a	21 ^a
Grape	0.1	0.59	0.33	0.347	0.67
Must	< 0.04	< 0.05	< 0.01	< 0.05	< 0.05
Wine	< 0.04	< 0.01	< 0.01	< 0.01	< 0.01
Pf must/juice	< 0.4	< 0.085	< 0.030	< 0.144	< 0.075
Pf wine	< 0.4	< 0.017	< 0.030	< 0.029	< 0.015

^a White grapes

The median processing factors for must and wine are < 0.08 and < 0.023 mg/kg based on samples collected at the recommended PHI. The Meeting estimated STMR values of 0.0020 mg/kg and 0.00072 mg/kg for must and wine, respectively.

Raisins were prepared from the harvested grapes in two trials. However, the results are contradictory (the calculated processing factors were 2.26 and 0.417) and a processing factor could not be calculated.

Strawberries

Strawberry samples, taken 3 days after last pesticide treatment with dinocap, were processed to jam and preserve with a procedure resembling commercial practice. The residues measured in RAC and processed products are summarised below.

Dosage kg ai/ha & appl. No	0.4–0.41 × 6	0.39–0.42 × 6	0.21–0.22 × 3	0.20–0.21 × 3
Strawberry fruits (unwashed)	0.23	0.31	0.07	0.13
Jam	0.079	0.07	< 0.01	0.06
Preserve	< 0.05	0.11	< 0.01	0.11
Pf for jam	0.34	0.23	< 0.14	0.46
Pf for preserve	< 0.22	0.35	< 0.14	0.85

The calculated median processing factor for both jam and preserve is 0.285. The Meeting estimated an STMR value of 0.024 for strawberry jam and preserve.

Residues in animal commodities

Animal metabolism studies performed with dinocap evaluated by previous Meetings of the JMPR revealed that no radioactive residues were detectable in milk or tissues at any dose level (0.1–1 ppm). Consequently animal feeding studies are not required.

RECOMMENDATIONS

On the basis of the data from supervised trials, the Meeting concluded that the residue concentrations listed below are suitable for establishing MRLs and for assessing IEDIs and IESTIs.

Definition of residue in plant commodities for enforcement purposes: dinocap, sum of isomers.

Definition of the residue for estimation of dietary intake: the sum of meptyldinocap and the corresponding phenol, 2,4-DNOP, expressed as the parent meptyldinocap.

CCN	Commodity	Proposed MRL (mg/kg)	STMR or STMR-P (mg/kg)
VC 0431	Squash, Summer	0.07 ^a	0.02
VC 0424	Cucumbers	0.07 ^a	0.02
FB 0269	Grapes	0.2 ^b	0.025
JF 0269	Grape juice		0.002
VC 0046	Melons, except watermelon	0.5 ^a	0.02
FB 0275	Strawberry	0.3 ^b	0.085
	Strawberry jam		0.024
	Strawberry preserve		0.024
	Wine		0.00072

^a: The maximum residue level accommodates the residues derived from the use of dinocap on fruiting vegetables, cucumbers. The Meeting recommended to reevaluate the current CXL of 0.05*.

^b: The current CXL of 0.5 mg/kg for dinocap covers the use of meptyldinocap as well.

DIETARY RISK ASSESSMENT

Long-term intake

The evaluation of meptyldinocap resulted in recommendations for MRLs and STMR values for raw and processed commodities. Where data on consumption were available for the listed food commodities, dietary intakes were calculated for the 13 GEMS/Food Consumption Cluster Diets. The results are shown in Annex 3 of the 2010 Report.

The IEDIs in the thirteen Cluster Diets, based on estimated STMRs were 0% of the maximum ADI (0.02 mg/kg bw). The Meeting concluded that the long-term intake of residues of difenoconazole from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

As the establishment of an ARfD was previously considered unnecessary, the Meeting concluded that short-term intake of meptyldinocap residues is unlikely to present a public health concern.

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