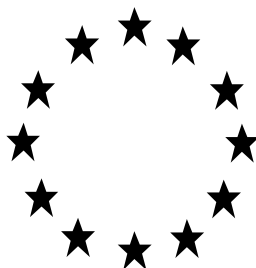


Draft Assessment Report



DIFENOCONAZOLE

Volume 3 **Annex B.1** **Identity**

Rapporteur Member State: Sweden

May 2006

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WARNING: This document forms part of an EC evaluation data package and should not be relied upon for registration. Registration must not be granted on the basis of this document.

B.1 Identity**B.1.1 Identity of the active substance (Annex IIA 1 and 3.1)****B.1.1.1 Name and address of the applicant for inclusion of the active substance in Annex I (Annex IIA 1.1)**

Applicant: Syngenta Ltd.
Priestley Road
Surrey Research Park
Guildford Surrey GU2 7YH
Great Britain

Contact point:

B.1.1.2 Manufacturer of active substance (Annex IIA 1.2)

Manufacturer:

Address:

Location of plant:

Contact Point:

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DIFENOCONAZOLE
Annex B.1: Identity

B.1.1.3 Common name and synonyms (Annex IIA 1.3)

ISO common name: Difenoconazole (published)

B.1.1.4 Chemical name (Annex IIA 1.4)

IUPAC: 1-[2-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-4-methyl[1,3]dioxolan-2-ylmethyl]-1H-[1,2,4] triazole

CA: 1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole

B.1.1.5 Manufacturer's development code number(s) (active substance) (Annex IIA 1.5)

Code no.	The period for which it was used	Remarks (e.g. which countries has the code been used in)
CGA 169374	From 1989-present (source the e-Pesticide Manual v. 3.1)	Used in all countries. The Ciba-Geigy code has been retained following the merger to Syngenta

B.1.1.6 CAS, EC and CIPAC numbers (Annex IIA 1.6)

CAS: 119446-68-3

EC: Not allocated

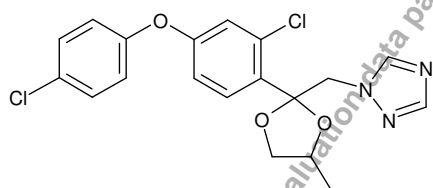
CIPAC: Not allocated

B.1.1.7 Molecular and structural formula, molecular mass (Annex IIA 1.7)

Molecular formula: C₁₉H₁₇Cl₂N₃O₃

Molecular mass: 406.3

Structural formula:

**B.1.1.8 Method of manufacture (Annex IIA 1.8)**

Details on the manufacturing methods are confidential information - See Annex C.

B.1.1.9 Specification of purity of the active substance (Annex IIA 1.9)

Technical active substance contains difenoconazole at a minimum of 940 g/kg (see Annex C for further details).

DIFENOCONAZOLE
Annex B.1: Identity

B.1.1.10 Identity of isomers, impurities and additives (Annex IIA 1.10)

Confidential information, see Annex C

B.1.1.11 Analytical profile of batches (Annex IIA 1.11)

Confidential information, see Annex C

B.1.1.12 Function (Annex IIA 3.1)

Fungicide

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DIFENOCONAZOLE
Annex B.1: Identity**B.1.2 Identity of the plant protection product (Annex IIIA 1)****B.1.2.1 Applicant (Annex IIIA 1.1)**

See B.1.1.1

B.1.2.2 Manufacturer of preparation and active ingredient (Annex IIIA 1.2)**B.1.2.2.1 Active substance**

See B.1.1.2.1

B.1.2.2.2 Preparation

Score 250 EC

Manufacturer:

[REDACTED]
[REDACTED]
[REDACTED]

Location of plant:

[REDACTED]

Contact Point:

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

DIFENOCONAZOLE
Annex B.1: Identity**Dividend 030 FS****Manufacturer:**

[REDACTED]
[REDACTED]
[REDACTED]

Location of plant:

[REDACTED]

Contact Point:

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

B.1.2.3 Current, former and proposed trade names and development code number (Annex III 1.3)**B.1.2.3.1 Current, former and proposed trade names**

The preparation A-7402 T has the following current trade names in EU: Bardos 250 EC (Austria), Geyser (Belgium and France), Geyser 250 EC (Luxembourg), Plover (UK), Score (France, Germany and Spain), Score 25 EC (Italy and Spain), Score 250 EC (Greece, Ireland, the Netherlands and Portugal) and Sico 250 EC (France)

The preparation A-9142 G has the following current trade names in the EU: Dividend (France, Hungary, Poland, Slovak Republic, Slovenia and Spain) and Dividend 030 FS (Danmark and Sweden)

B.1.2.3.2 Development code numbers

Code No.	Material
A-7402 T	Score 250 EC
A-9142 G	Dividend 030 FS

B.1.2.4 Composition of the preparations (Annex IIIA 1.4)**Score 250 EC**

content of pure active substance :	250 g / l	(23.2 % w / w)
limits :	235 – 265 g / l	(21.8 – 24.6 % w / w)
content of technical active substance :	260.4 g / l	(24.2 % w / w)
limits :	244.8 – 276 g / l	(22.7 – 25.7 % w / w)
at a <u>typical</u> purity of the technical active substance of 96 %		

Information on the formulants is confidential, see Annex C.

Dividend 030 FS

content of pure active substance :	30 g / l	(2.86 % w / w)
limits :	27 – 33 g / l	(2.6 – 3.1 % w / w)
content of technical active substance :	31.3 g / l	(2.98 % w / w)
limits :	28.1 – 34.4 g / l	(2.7 – 3.3 % w / w)
at a <u>typical</u> purity of the technical active substance of 96 %		

Information on the formulants is confidential, see Annex C.

B.1.2.5 Physical state and nature of preparation (Annex IIIA 1.5)**Score 250 EC**

Physical state: liquid

Nature: emulsifiable concentrate [Code: EC]

Dividend 030 FS

Physical state: liquid

Nature: flowable concentrate for seed treatment [Code: FS]

B.1.2.6 Function (Annex IIIA 1.6)**Score 250 EC**

Fungicide

Dividend 030 FS

Fungicide for seed treatment

DIFENOCONAZOLE
Annex B.1: Identity

B.1.3 References relied on

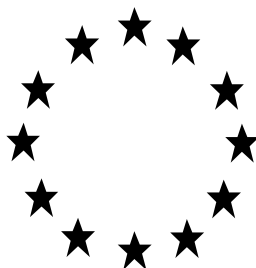
Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N*	Owner [†]
IIA 1.1-IIA 1.7	Baker, S.	2004a	Document M-II, section 1	N	SYN
IIA 1.9	Baker, S.	2004a	Document M-II, section 1	N	SYN
IIIA 1.1-IIIA 1.4	Baker, S.	2004b	Document MIII, section 1 (Score) Document MIII, section 1 (Dividend)	N	SYN
IIIA 1.3	Poyntz, B.	2004	Document D-2	N	SYN
IIIA 1.5-IIIA 1.6	Baker, S.	2004b	Document MIII, section 1 (Score) Document MIII, section 1 (Dividend)	N	SYN

* Protection for 5 years claimed from date of decision concerning listing in Annex I - the study report has not been submitted any of the Member States in support of an application for authorization, or (though the study report has been submitted) has not been used any of the Member States as the basis for decision on the initial authorization, or to maintain a given authorization, of a plant protection product before the date of submission of the dossier to Rapporteur Member State.

[†] Owners' code identifications and names (Code identification: SYN, Name: Syngenta Limited)

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Draft Assessment Report



DIFENOCONAZOLE

Volume 3

Annex B.2

Physical and chemical properties

Rapporteur Member State: Sweden

May 2006

KEMI

KEMIKALIEINSPEKTIONEN
SWEDISH CHEMICALS INSPECTORATE

Volume 1

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B.2 Physical and chemical properties

B.2.1 Physical and chemical properties of the active substance (Annex IIA 2)

B.2.1.1 Melting point and boiling point (Annex IIA 2.1)

B.2.1.1.1 Melting point (Annex IIA 2.1.1)

Reference: *Das, R. 1999a*
Test Material: Difenoconazole PAI, Batch No.: AMS 255/3, purity 99.3%
Method: EEC A.1, OECD 102, OPPTS 830.7200
Results: 82.0 °C-83.0 °C. With an estimated accuracy of ± 0.4 °C
RMS comments: The method and the result are acceptable.

B.2.1.1.2 Boiling point (Annex IIA 2.1.2)

Reference: *Das, R. 1997*
Test Material: Difenoconazole PAI, Batch No.: AMS 255/3, purity 99.3%
Method: EEC A.2, OECD 103, OPPTS 830.7220 (The method of Siwoloboff)
Results: Difenoconazole decomposes before boiling at atmospheric pressure.
From the vapour pressure study (see B.2.1.3.1) it is given that difenoconazole would boil at 100.8 °C at a reduced pressure of 3.7 mPa.
RMS comments: The methods and the results are acceptable.

B.2.1.1.3 Temperature at which decomposition or sublimation occurs (Annex IIA 2.1.3)

Reference: *Das, R. 1997*
Test Material: Difenoconazole PAI, Batch No.: AMS 255/3, purity 99.3%
Method: EEC A.2, OECD 103, OPPTS 830.7220 (DSC)
Results: Decomposition begins at about 337 °C

Reference: *Schürch, H. 1993*
Test Material: Difenoconazole technical, Batch No.: P.807002, purity 91.3%
Method: OECD 113 (DTA)
Results: No thermal effect was found between room temperature and 150 °C, except melting when heated both in air and in the absence of air.

RMS comments: The methods used in both studies and the results therein are acceptable.

B.2.1.2 Relative density (Annex IIA 2.2)

Reference: *Füldner, H. H. 1999*
Test Material: Difenoconazole PAI, Batch No.: AMS 255/3, purity 99.3%
Method: OECD 109 (air comparison pycnometer)
Results: $\rho = 1.39 \pm 0.04 \times 10^3 \text{ kg/m}^3$ at 22 °C corresponding to a relative density of 1.39
RMS comments: The density is determined at 22 °C instead of 20 °C, which means that the relative density which should be given as D_4^{20} might be somewhat lower than the reported value of 1.39.
However the expected deviation is probably within the reported error of ± 0.04 .
The method and the results are therefore acceptable.

B.2.1.3 Vapour pressure and volatility (Annex IIA 2.3)

B.2.1.3.1 Vapour pressure (Annex IIA 2.3.1)

Reference: *Rordorf, B. 1988*
Test Material: Difenoconazole PAI, Batch No.: AMS 255/102, purity 99.0%
Method: EEC A.4, OECD 104 (gas saturation method)
Results: The vapour pressure for difenoconazole was determined to be:
 $3.32 \times 10^{-8} \text{ Pa}$ at 25 °C

Obtained by extrapolating the vapour pressure curve $^{10}\log P [\text{Pa}] = 18.396 - 7714.5 \times 1/T [\text{K}]$ for the solid state, which was calculated from the experimentally derived vapour pressure curve for the liquid phase (obtained by fitting data from measurements between 78.1 °C and 181.1 °C).

Reference: *Krohn, J. 2001a*
Test Material: 1H-1,2,4-triazol (CGA 71019; metabolite of difenoconazole; see table B.2.1.16-2 for identity details), purity 99.7%
Method: OECD 104 (vapour pressure balance)
Results: The vapour pressure for the metabolite CGA 71019, was determined to be:
 $3.4 \times 10^{-1} \text{ Pa}$ at 25 °C

Obtained by extrapolating the vapour pressure curve which was experimentally derived by fitting data from measurements between -14 °C and 46 °C.

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Reference: *Widmer, H., 2001a*

Test Material: 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-[1,2,4]triazol-1-yl-ethanol (CGA 205375; metabolite of difenoconazole; see table B.2.1.16-2 for identity details), purity 99%

Method: EEC A.4, OECD 104

Results: The vapour pressure for the metabolite CGA 205375 was determined by direct measurement to be:
 $<5.0 \times 10^{-6}$ Pa at 25 °C

RMS comments: The first study (Rordorf, B. F., 1988) and the second study (Krohn, J. 2001a) were not performed in accordance with GLP. This should however not have affected the quality of the results.

The vapour pressure of the metabolite CGA 205375 (study 3; Widmer, H., 2001a) was determined by direct measurement instead of extrapolation. The reported value is therefore a threshold value, since the vapour pressure was too low to be measured by the analytical method employed (HPLC).

In conclusion, all three studies are acceptable.

B.2.1.3.2 Volatility (Henry's law constant; Annex IIA 2.3.2)

Reference: *Burkhard, N. 1998*

Method: The Henry's law constant of difenoconazole was obtained by calculations using the vapour pressure (see B.2.1.3.1) and the water solubility (see B.2.1.6)

Results: $H_{\text{difenoconazole}} = 9.0 \times 10^{-7} \text{ Pa} \times \text{m}^3 \times \text{mol}^{-1}$

Reference: *Krohn, J. 2001b*

Method: The Henry's law constant of the metabolite 1H-1,2,4-triazol (CGA 71019) was obtained by calculations using the vapour pressure (see B.2.1.3.1) and the water solubility (see B.2.1.6)

Results: $H_{\text{CGA 71019}} = 2 \times 10^{-5} \text{ Pa} \times \text{m}^3 \times \text{mol}^{-1}$ at 20 °C
 $H_{\text{CGA 71019}} = 3 \times 10^{-5} \text{ Pa} \times \text{m}^3 \times \text{mol}^{-1}$ at 25 °C

RMS comments: Study 2 (Krohn, J. 2001b) was not submitted by the applicant to address this parameter (i.e. it is submitted to address the water solubility), but as it gives useful information it is included here. Further, the result is based on the open literature value for the solubility of 1,2,4-triazol (see B.2.1.6).

In overall both studies are acceptable.

WARNING: This document forms part of an ECHA evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

B.2.1.4 Appearance (Annex IIA 2.4)

B.2.1.4.1 Colour and physical state (Annex IIA 2.4.1)

Purified active substance

Reference: *Das, R. 1999b*
Test Material: Difenoconazole PAI, Batch No.: AMS 255/3, purity 99.3%
Method: Visual inspection
Results: Difenoconazole was determined to be a white fine crystalline powder at 25 °C.

Technical active substance

Reference: *Das, R. 1993*
Test Material: Difenoconazole TGAI, Batch No.: V 7, purity not stated
Method: Visual assessment
Results: Difenoconazole technical was determined to be an off-white powder.

RMS comments: The temperature employed and the used purity of the test material in the assessment of the technical material (Das, R. 1993) is not stated. Both studies are still acceptable.

B.2.1.4.2 Odour (Annex IIA 2.4.2)

Purified active substance

Reference: *Das, R. 1999b*
Test Material: Difenoconazole PAI, Batch No.: AMS 255/3, purity 99.3%
Method: Organoleptic
Results: Difenoconazole was determined to be odourless.

Technical active substance

Reference: *Das, R. 1993*
Test Material: Difenoconazole TGAI, Batch No.: V 7, purity not stated
Method: Organoleptic
Results: The odour for the technical material was determined to be slightly sweet.

RMS comments: The temperature employed and the used purity of the test material in the assessment of the technical material (Das, R. 1993) is not stated. Both studies are still acceptable.

WARNING: This document forms part of an ECV evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

B.2.1.5 Spectra and structural analysis (Annex IIA 2.5)

B.2.1.5.1 Spectra and structural analysis for the active substance (Annex IIA 2.5.1)

Reference: *Oggenfuss, P. 1999*

Test Material: Difenoconazole PAI, Batch No.: AMS 255/3, purity 99.3%

B.2.1.5.1.1 UV/VIS spectrometry

Method UV/VIS

Cell path length: 1 cm

Cell type : quartz

Solvent: methanol

Results: Acidic conditions (100 ml methanol/1N HCl; 91:9); sample concentration 0.0141 mg/mL

$\lambda_{\max}[\text{nm}]$	Molar extinction coefficient [$\text{l x mol}^{-1} \text{ x cm}^{-1}$]
215	29306
235	17556
275	1743

Neutral conditions: sample concentration 0.0141 mg/mL

$\lambda_{\max}[\text{nm}]$	Molar extinction coefficient [$\text{l x mol}^{-1} \text{ x cm}^{-1}$]
215	28658
235	17392
275	1680

Alkaline conditions (100 ml methanol/1N NaOH; 91:9); sample concentration 0.0141 mg/mL

$\lambda_{\max}[\text{nm}]$	Molar extinction coefficient [$\text{l x mol}^{-1} \text{ x cm}^{-1}$]
220	21210
235	17176
275	1542


No absorption maximum between 300 nm and 750 nm was observed at any pH.

B.2.1.5.1.2 IR spectrometry

Method: IR

Sample preparation: KBr-pellet

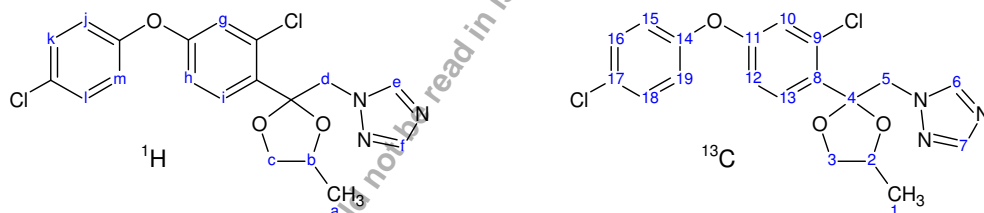
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Results:	Wavenumber [cm ⁻¹]	Assignment
	ca. 3000	C-H stretch
	1606, 1585	C=N stretch in heterocycle
	1508, 1478	Aromatic C-C, and C-N stretch
	1226	C-O-C stretch asymmetric
	1274, 1138, 1089, 1048	C-O-C stretch in 

B.2.1.5.1.3 NMRMethod: ¹H- and ¹³C-NMR

Nucleus:	¹ H	¹³ C
Frequency (MHz):	300	75
Solvent:	CDCl ₃	CDCl ₃
Internal standard:	TMS	-
Temperature (K)	ambient	ambient

Results:



Chemical shift (ppm)	Assignment	Number of protons
Proton-NMR		
1.1-1.2	a	3
3.0-3.4	b	1
3.9-4.2	c	2
4.6-4.9	d	2
6.8-7.7	g, h, i, j, k, l, m	7 (1 each)
7.8-8.3	e & f	2 (1 each)
Carbon-NMR		
18	1	
54	5	
72-75	2 & 3	
107	4	
116	12	
120-122	10 & 15 & 19	
129-134	8 & 9 & 13 & 16 & 17 & 18	
145, 151	6 & 7	

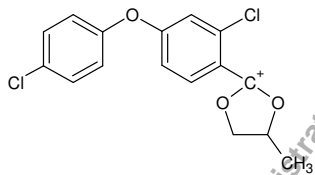
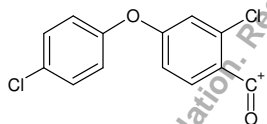
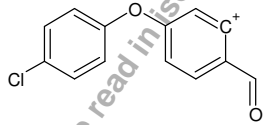
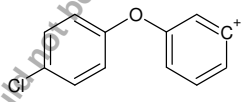
DIFENOCONAZOLE
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154, 158	11 & 14
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B.2.1.5.1.4 Mass spectrometry

Method: MS (Ion trap-EI)

Results:

m/z	Fragment ion
405	M ⁺ , molecular ion (not detected)
323	
265	
230	
202	

RMS comments: All the results from the spectral analysis support the proposed structure for difenoconazole.

B.2.1.5.2 Spectra and structural analysis for significant impurities (Annex IIA 2.5.2)

None of the impurities are considered to have toxicological or ecotoxicological significance.

B.2.1.6 Solubility in water (Annex IIA 2.6)

Reference: *Stulz, J. 1994*

Test Material: Difenoconazole PAI, Batch No.: AMS 255/102, purity 99.0%

Method: EEC A.6, OECD 105 (shake-flask method)

Results: The solubility of difenoconazole in water at 25 °C ± 0.1 °C was determined to be:
15 mg/l ± 1.3 mg/l at a pH of approximately 7.2.

Difenoconazole does not dissociate at environmentally relevant pH and the solubility in water should therefore not be affected by a pH change in the interval pH 4-10. Both isomers of difenoconazole (cis/trans) had about the same solubility in water.

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- Reference: *Krohn, J. 2001b*
- Test Material: 1H-1,2,4-triazol (CGA 71019; metabolite of difenoconazole; see table B.2.1.16-2 for identity details)
- Method: The solubility of the triazol in water in g/l is calculated from the solubility in water expressed in mole fractions, which were found in literature.
- Results: The solubility of the metabolite CGA 71019 in water was calculated to be:
700 g/l at 20 °C
730 g/l at 25 °C
- Reference: *Das, R. 2001a*
- Test Material: 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-[1,2,4]triazol-1-yl-ethanol (CGA 205375; metabolite of difenoconazole; see table B.2.1.16-2 for identity details), purity 99%
- Method: EEC A.6, OECD 105 (shake-flask method)
- Results: The solubility of the metabolite CGA 205375 in water at 25 °C ± 0.1 °C was determined to be:
12 mg/l ± 0.4 mg/l at a pH of approximately 7.7.
- RMS comments: The metabolite CGA 205375 (see study three, Das, R. 2001a) might be slightly acidic, which means that the solubility in water might increase at higher pH.
In overall all three studies are acceptable.

B.2.1.7 Solubility in organic solvents (Annex IIA 2.7)

- Reference: *Kettner, R. 1999a*
- Test Material: Difenoconazole TGAI, Batch No.: WM 806228, purity 94.6%
- Method: CIPAC MT 157.3
- The solubility in different organic solvents at 25 °C was determined to be:

acetone:	>500 g/l
dichloromethane:	>500 g/l
ethyl acetate:	>500 g/l
hexane:	3.0 g/l
methanol:	> 500 g/l
octanol:	110 g/l
toluene	>500 g/l

- RMS comments: The method and the results are acceptable.

B.2.1.8 Partition coefficient, log P_{ow} (Annex IIA 2.8)

Reference: *Kettner, R. 1999b*

Test Material: Difenoconazole PAI, Batch No.: AMS 255/3, purity 99.3%

Method: EEC A.8, OECD 107, OPPTS 830.7550 (shake flask method)

Results: The following result was obtained for difenoconazole:
log P_{ow}=4.36 ± 0.02 at 25 °C and a pH of approximately 8 (unbuffered distilled water).

Reference: *Widmer, H 2005*

Test Material: 1,2,4-triazol (CGA 71019; metabolite of difenoconazole; see table B.2.1.16-2 for identity details), purity 99%

Method: EEC A.8 (shake flask method)

Results: The following result was obtained for the metabolite CGA 71019 in buffered solutions at 25°C:
log P_{ow}= -0.62 at pH 5
log P_{ow}= -0.71 at pH 7
log P_{ow}= -0.68 at pH 9

Reference: *Das, R. 2001b*

Test Material: 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-[1,2,4]triazol-1-yl-ethanol (CGA 205375; metabolite of difenoconazole; see table B.2.1.16-2 for identity details), purity 99%

Method: EEC A.8, OECD 107, OPPTS 830.7550 (shake flask method)

Results: The following result was obtained for the metabolite CGA 205375:
log P_{ow}=3.81 at 25 °C and a pH of approximately 8 (unbuffered distilled water).

RMS comments: The determination in the first study (Kettner, R. 1999) was only performed at one pH since difenoconazole does not dissociate at environmentally relevant pH.

In the second study (Widmer, H. 2005) the concentration in the aqueous phase of some mixtures slightly exceeded the limit (0.01 mol/litre) specified in the method (EEC A.8).

However, the standard deviations of the measurements were low and the study is therefore considered acceptable.

In overall all three studies and the results thereof are acceptable.

B.2.1.9 Stability in water (Annex IIA 2.9)

B.2.1.9.1 Hydrolysis rate (Annex IIA 2.9.1)

Reference: Atkins, R. H. **1991**

Test Material: Radiolabelled difenoconazole (uniformly ^{14}C -labelled in the triazol-ring) with a radiochemical purity of 99.2%

Method: Sterile solutions of radiolabelled difenoconazole were stored for 30 days at pH 5, 7 and 9 and a temperature of 25 °C.

Samples were taken at 0, 2, 7, 12, 16, 19, 23 and 27 days and finally at the end of the testing time. Recoveries were determined by radio assay (liquid scintillation spectrometer). Quantitative analysis was done by HPLC (fitted both with a UV and a radioactivity detector).

GC-MS were used for structural analysis of degradates.

Results: After 30 days of incubation at 25 °C 95.2%, 100.5% and 101.9% of added radiocarbon remained as difenoconazole.

The calculated half-lives for difenoconazole were significantly greater than 30 days (> 1000 days). Only two degradates (unknown) were detected throughout the study and in quantities <1.2% of applied radiocarbon.

RMS comments: The method and the results are acceptable.

B.2.1.9.2 Photochemical transformation (Annex IIA 2.9.2)

Reference: *Gaauw, van der A.* **2002**

Test Material: Radiolabelled difenoconazole (uniformly ^{14}C -labelled in the triazol-ring) with a radiochemical purity of 99.2%

Method: SETAC: Society of Environmental Toxicology and Chemistry "Procedure for Assessing the Environmental Fate and Ecotoxicology of Pesticides; March 1995

OECD/GD(97)21: Guidance Document on Direct Phototransformation of Chemical in Water OPPTS 835.2210

Solutions of radiolabelled difenoconazole were irradiated with artificial sunlight (xenon arc light) at 25 °C and pH 7 for 15 days.

Samples were taken at 0, 3, 6, 8 and 10 days and at the end of the testing period.

Recoveries were determined by radio assay (liquid scintillation counter). Quantitative analysis was done by HPLC.

Results: Difenoconazole was considered to be stable towards photolysis since 90.9% of the applied radioactivity was present as the parent compound at the end of the irradiation period. Besides difenoconazole, three unknown degradates were present but none exceeded 6.3% of applied

radioactivity.

RMS comments: The result is in good agreement with the fact that difenoconazole has a very low absorption above 290 nm (see B.2.1.5.1.1).

The method and the result are acceptable.

B.2.1.9.3 Quantum yield (Annex IIA 2.9.3)

Reference: *Hennecke, D. 2002*

Test Material: Difenoconazole PAI, Batch No.: AMS 255/3, purity 99.3%

Method: A three tiered approach according to the "Draft OECD Test Guideline: Phototransformation of Chemicals in Water, Direct and Indirect Photolysis" was used.

The quantum yield, which was experimentally determined, was used to calculate theoretical half-lives at various seasons.

Results: The quantum yield was determined to be $1.55 \times 10^{-2} \pm 0.11 \times 10^{-2}$. The calculated half-lives of difenoconazole in water bodies at various seasons for 53 °N are summarized in table B.2.1.9.3 below. The minimal, normal and maximum half-lives are based on seasonal and weather variations for the respective month. As shown, photolysis is considered to be an insignificant process for degradation of difenoconazole in surface water.

Table B.2.1.9.3: Summary of expected environmental half-life values (in years) for difenoconazole

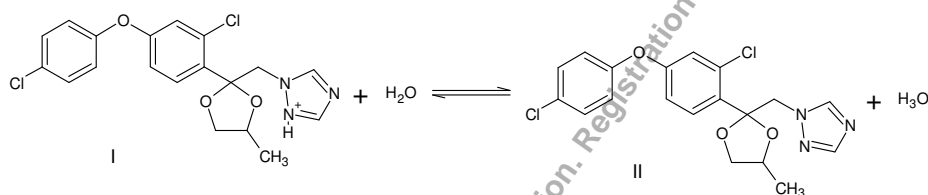
Month	Minimal	Normal	Maximal
January	>10000	>10000	>10000
February	5085.5	>10000	>10000
March	282.0	535.8	2232.6
April	38.3	68.9	275.5
May	15.4	24.6	98.5
June	9.0	13.5	54.1
July	7.8	11.8	39.2
August	9.5	14.3	47.7
September	28.9	49.1	181.8
October	168	320.7	1457.6
November	8499.3	>10000	>10000
December	>10000	>10000	>10000

RMS comments: The results are in good agreement with that determined in the photolysis study (see B.2.1.9.2).

The method and the results are acceptable.

B.2.1.9.4 Dissociation constant (pKa; Annex IIA 2.9.4)

Reference: Hörmann, A. **1999**
Test Material: Difenoconazole PAI, Batch No.: AMS 255/3, purity $99.3 \pm 0.3\%$
Method: OECD 112 (titration method)
Results: pKa for the deprotonation of the triazole (see below) was determined to be:
 1.07 ± 0.18



This means that at pH < 1.1, the protonated form I is predominately present, whereas at pH > 1.1 the non-ionised form II predominates.

RMS comments: The standard deviation of the determination was higher than the highest allowed by the method (0.1). However the obtained pKa value is low enough to have low or no environmental relevance.

The method and the results are therefore acceptable.

B.2.1.10 Stability in air, photochemical oxidative degradation, identity of breakdown product(s) (Annex IIA 2.10)

Reference: Stamm, E. **1998**
Test Material: Difenoconazole, structural formula
Method: Calculations according to the method of Atkinson by the use of a commercially available data program.
Results: The overall degradation rate constant for difenoconazole was calculated to be:
 $26.4 \times 10^{-12} \text{ cm}^3/\text{molecule-sec.}$
Half-life = 4.87 days

B.2.1.11 Flammability and auto-flammability (Annex IIA 2.11)

B.2.1.11.1 Flammability (Annex IIA 2.11.1)

Reference: Schürch, H. **1992a**
Test Material: Difenoconazole TGAI, Batch No.: P.807002, purity 91.8%, moisture content 0.2%

Method: EEC A.10
Results: The test material should not be considered highly flammable.
RMS comments: The method and the result are acceptable.

B.2.1.11.2 Auto-flammability (Annex IIA 2.11.2)

Reference: *Schürch, H. 1992b*
Test Material: Difenoconazole TGAI, Batch No.: P.807002, purity 91.8%
Method: EEC A.16
Results: The test material did not self-ignite below 78 °C (melting point).
RMS comments: The method and the results are acceptable.

B.2.1.12 Flash point (Annex IIA 2.12)

Not applicable since the melting point is >40 °C

B.2.1.13 Explosive properties (Annex IIA 2.13)

Reference: *Schürch, H. 1992c*
Test Material: Difenoconazole TGAI, Batch No.: P.807002, purity 91.8%, moisture content 0.2%
Method: EEC A.14
Results: Not explosive.
RMS comments: The used material has a lower purity than the specification of the technical material (i.e. 94%). However, since the result was negative this is acceptable.

B.2.1.14 Surface tension (Annex IIA 2.14)

Reference: *Martin, N. 1999*
Test Material: Difenoconazole TGAI, Batch No.: WM 806228, purity 94.6%
Method: EEC A.5, OECD 115 (ring method), ISO 304
Results: The surface tension at 20 °C of a 90% saturated solution of difenoconazole in distilled water was determined to be:
62.8 mN/m

Difenoconazole is therefore not surface active.
RMS comments: The method and the results are acceptable.

B.2.1.15 Oxidizing properties (Annex IIA 2.15)

Reference: *Schürch, H. 1992d*
Test Material: Difenoconazole TGAI, Batch No.: P.807002, purity 91.8%
Method: EEC A.17
Results: Difenoconazole is not an oxidizer.
RMS comments: The used material has a lower purity than the specification of the technical material (i.e. 94%). However, since the result was negative this is acceptable.

B.2.1.16 Summary and evaluation of data presented under points B.2.1.1 to B.2.1.15

Study reports with regard to physical and chemical properties of the active substance have been submitted for all reported parameters.

All tests have been performed according to the methods recommended in Annex II of the directive 91/414/EEC except the hydrolysis rate, which was determined by an in-house method. Furthermore, all of the tests have been performed in accordance with GLP, except the vapour pressures for difenoconazole and the metabolite CGA 71019. All the tests and the methods used are considered acceptable.

Difenoconazole as manufactured is an off-white powder with a slightly sweet odour. The relative density is 1.39 and the pure material has a melting point of 82-83 °C. The solubility is not pH dependant under environmentally relevant pH and was measured to be approximately 15 mg/l at pH 7.2 and the log P_{ow} was determined to be 4.36 at pH 8. It is stable towards both hydrolysis and photolysis. The half-life of difenoconazole in the reaction with OH-radicals in the atmosphere is 4.9 days.

Difenoconazole technical has no explosive or oxidizing properties and should not be regarded as highly flammable or auto-flammable.

The physical-chemicals properties of difenoconazole are summarized in table B.2.1.16-1.

Moreover, some physical and chemical parameters were determined for the relevant metabolites CGA 71019 and CGA 205375 which are summarized in table B.2.1.16-2.

DIFENOCONAZOLE
Annex B.2: Physical and chemical properties

Table B.2.1.16-1: Summary of the physical and chemical properties of difenoconazole

Identity, chemical and physical properties	Results	Study document available	EEC method or equivalent	GLP	Comments
CAS No.:	119446-68-3				
EEC No.:	Not allocated				
CIPAC No.:	Not allocated				
Molecular formula	C ₁₉ H ₁₇ Cl ₂ N ₃ O ₃				
Molecular mass	406.3				
Melting point	82 °C-83 °C	Y	EEC A.1 OECD 102, OPPTS 830.7200	Y	
Boiling point	Decomposes before boiling at atmospheric pressure Boiling point at reduced pressure (3.7 mPa): 100.8 °C	Y	EEC A.2 OECD 103 OPPTS 830.7220	Y	
Temperature at which decomposition or sublimation occurs	Decomposition begins at about 337 °C No thermal effect, except melting, was found between room temperature and 150 °C	Y	EEC A.2 OECD 103 OPPTS 830.7220 OECD 113	Y	
Relative density, D_4^{20}	1.39	Y	OECD 109	Y	
Vapour pressure, Pa	3.32 x 10 ⁻⁸ Pa at 25 °C	Y	EEC A.4, OECD 104	N	Extrapolated from the vapour pressure curve
Henry's law constant Pa·m³/mole at 20°C	H=9.0 x 10 ⁻⁷	Y	Calc.		
Physical state and appearance	<u>PAI</u> White fine crystalline powder <u>TGAI</u> Off-white powder	Y	Visual inspection Visual assessment	Y	
Odour	<u>PAI</u> Odourless <u>TAI</u> Slightly sweet	Y	Organoleptic	Y	
Spectra and structural analysis of the active ingredient		Y		Y	All the results from the spectral analysis support the proposed structure for difenoconazole
NMR	¹ H- and ¹³ C-spectra in support of structure				
IR	Spectra in support of structure				
UV/VIS	Maxima under acidic conditions: 215 nm (ε =29306) 235 nm (ε =17556) 275 nm (ε =1743) Maxima in unadjusted distilled water: 215 nm (ε =28658) 235 nm (ε =17392) 275 nm (ε =1680)				


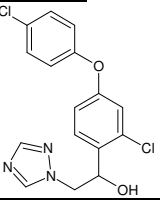
DIFENOCONAZOLE
Annex B.2: Physical and chemical properties

Identity, chemical and physical properties	Results		Study document available	EEC method or equivalent	GLP	Comments
	Maxima under alkaline conditions: 220 nm (ε =21210) 235 nm (ε =17176) 275 nm (ε =1542)					
Mass-spectra	Peaks at 323, 265, 230 and 202 support the structure of difenoconazole					
Spectra and structural analysis for significant impurities	None of the impurities are considered to have toxicological or ecotoxicological significance.					
Solubility in water at 25 °C	15 mg/l at a pH of 7.2		Y	EEC A.6, OECD 105	Y	
Solubility in Annex II recommended organic solvent groups at 20 °C	<u>Solvent</u>	<u>Solubility [g/l]</u>	Y	CIPAC MT 157.3	Y	
	acetone	>500				
	dichloromethane	>500				
	ethyl acetate	3.0				
	hexane	3.0				
	methanol	51				
	octanol	110				
	toluene	>500				
Partition coefficient, n-octanol/water, log P _{ow}	4.36 ± 0.02 at pH 8		Y	EEC A.8, OECD 107, OPPTS 830.7550	Y	
Hydrolysis rate, DT ₅₀ (days), at pH 5, 7 and pH 9	No significant hydrolysis (<10 %) was observed at pH 5, 7 and 9 after 30 days at 25 °C.		Y	In-house method	Y	
Direct phototransformation in water, DT ₅₀ (days), at pH 7 and 25 °C ± 1 °C	No significant photolysis was observed after 15 days of irradiation.		Y	OECD/GD(97)21, OPPTS 835.2210	Y	
Quantum yield	Quantum yield was determined to be: 1.55 x 10 ⁻² The theoretical lifetime of difenoconazole in upper surface water was estimate to range between 9.5 years and 10000 years depending on season. Photolysis is considered to be an insignificant process for degradation of difenoconazole in surface water.		Y	Draft OECD Test Guideline: Phototransformation of Chemicals in water, Direct and Indirect Photolysis	Y	
Dissociation constant	The pKa for deprotonation of the triazole moiety of difenoconazole was determined to be: 1.07 ± 0.18		Y	OECD 112	Y	Standard deviation slightly higher than allowed by the method. Still acceptable
Photochemical oxidative degradation	Overall rate constant: 26.4 x 10 ⁻¹² cm ³ /molecule-sec. Half-life=4.87 days		Y	Calc.		
Flammability, °C	Not highly flammable		Y	EEC A.10	Y	

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Identity, chemical and physical properties	Results	Study document available	EEC method or equivalent	GLP	Comments
Auto-flammability, °C	Does not self-ignite below 78 °C (melting point)	Y	EEC A.16	Y	
Flash point, ° C	Not applicable, since the melting point is above 40°C				
Explosive properties	Not explosive	Y	EEC A.14	Y	
Surface tension, mN/m	For a 90% saturated solution: 62.8 mN/m at 20 °C Not surface active material	Y	EEC A.5, OECD 115, ISO 304	Y	
Oxidizing properties	No oxidizing properties	Y	EEC A.17	Y	

Table B.2.1.16-2: Summary of physical and chemical properties determined on the metabolites CGA 71019 and CGA 205375

Physical and chemical property	Result	Study document available	EEC method or equivalent	GLP	Comments
Identity CGA 71019	<u>Chemical name (CA)</u> 1H-1,2,4-Triazole <u>CAS No.</u> 288-88-0 <u>EC No.</u> 206-022-9 <u>Structure</u> 	-	-	-	
Identity CGA 205375	<u>Chemical name (IUPAC)</u> 1-[2-Chloro-4-(4-chloro-phenoxy)-phenyl]-2-[1,2,4]triazol-1-yl-ethanol <u>CAS No.</u> Not allocated <u>EC-No.</u> Not allocated <u>Structure</u> 	-	-	-	
Vapour pressure, Pa	<u>CGA 71019:</u> 3.4×10^{-1}	Y	OECD 104	N	
	<u>CGA 205375:</u> $<5.0 \times 10^{-6}$	Y	EEC A.4, OECD 104	Y	
Solubility in water	<u>CGA 71019:</u> 700 g/l at 20 °C 730 g/l at 25 °C	Y	Calculations based on literature values	-	

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	<u>CGA 205375:</u> 12 ± 0.4 mg/l at 25 °C and pH 7.7	Y	EEC A.6, OECD 105	Y	
Henry's law constant, Pa x m³ x mol⁻¹	<u>CGA 71019:</u> H=2 x 10 ⁻⁵ at 20 °C H=3 x 10 ⁻⁵ at 25 °C	Y	Calculations based on literature values	-	
Partition coefficient, log P_{ow}	<u>CGA 71019:</u> log P _{ow} = -0.62 at pH 5 log P _{ow} = -0.71 at pH 7 log P _{ow} = -0.68 at pH 9	Y	EEC A.8 (shake flask method)	Y	
	<u>CGA 205375:</u> log P _{ow} = 3.81 at 25 °C and a pH of approximately 8	Y	EEC A.8, OECD 107, OPPTS 830.7550 (shake flask method)	Y	

B.2.2 Physical, and technical properties of the plant protection product (Annex IIIA 2)

Product trade name	Product code number	Concentration of active substance
Score 250 EC	A-7402 T	250 g/l
Dividend 030 FS	A-9142 G	30 g/l
-	A-7402 G	250 g/l See Annex C for further details on this formulation

B.2.2.1 Appearance (Annex IIIA 2.1)

B.2.2.1.1 Colour and physical state

B.2.2.1.1.1 Colour and physical state of Score 250 EC

Reference: *Krips, H. J. 1998b*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: Visual observation

Results: The formulation is a clear yellow to brown liquid.

RMS comments: The method is acceptable

B.2.2.1.1.2 Colour and physical state of Dividend 030 FS

Reference: *Kalt, R. 1999a*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: Visual observation

Results: The formulation was assessed to be a red liquid at room temperature

RMS comments: The test is not performed in accordance with GLP. This should however not have affected the quality of the result. The method is therefore acceptable.

B.2.2.1.2 Odour

B.2.2.1.2.1 Odour of Score 250 EC

Reference: *Krips, H. J. 1998c*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: Organoleptic
Results: The formulation was assessed to have a penetrating odour.
RMS comments: The method is acceptable.

B.2.2.1.2.2 Odour of Dividend 030 FS

Reference: *Kalt, R. 1999a*
Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l
Method: Organoleptic
Results: The formulation exhibited a sweetish, chalky odour.
RMS comments: The test is not performed in accordance with GLP. This should however not have affected the quality of the result. The method is therefore acceptable.

B.2.2.2 Explosivity and oxidizing properties (Annex IIIA 2.2)

B.2.2.2.1 Explosive properties (Annex IIIA 2.2.1)

B.2.2.2.1.1 Explosive properties of Score 250 EC

Reference: *Krips, H. J. 1998c*
Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l
Method: EEC A.14
Results: The formulation is not explosive.
RMS comments: The method and the result are acceptable.

B.2.2.2.1.2 Explosive properties of Dividend 030 FS

Reference: *Angly, H. 1999a*
Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l
Method: EEC A.14
Results: The formulation is not explosive.
RMS comments: The method and the result are acceptable.

B.2.2.2.2 Oxidizing properties (Annex IIIA 2.2.2)

B.2.2.2.2.1 Oxidizing properties of Score 250 EC

Reference: *Angly, H. 1999*

Test Material: A-7402 G, Batch No.: P.706093, concentration of active substance: 265 g/l

Method: According to Recommendation on the Transport of Dangerous Goods, Manual of Test and Criteria. Part III, section 34. United Nations, 1995

Results: The product is not considered an oxidizing substance, and is therefore not considered a Division 5.1 substance.

RMS comments: The test was not performed according to EEC method A.17, since it is only applicable to solids. The method and the result are acceptable.

B.2.2.2.2.1 Oxidizing properties of Dividend 030 FS

Reference: *Angly, H. 1999b*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: According to Recommendation on the Transport of Dangerous Goods, Manual of Test and Criteria. Part III, section 34. United Nations, 1995

Results: The product is not considered an oxidizing substance, and is therefore not considered a Division 5.1 substance.

RMS comments: The test was not performed according to EEC method A.17, since it is only applicable to solids. The method and the result are acceptable.

B.2.2.3 Flash point, flammability and auto-flammability (Annex IIIA 2.3)

B.2.2.3.1 Flash point

B.2.2.3.1.1 Flash point of Score 250 EC

Reference: *Krips, H. J. 1998d*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: EEC A.9 (Pensky-Martens closed cup apparatus)

Results: The flash-point was determined to be: 63 °C at 101.3 kPa.

RMS comments: The method and the result are acceptable.

B.2.2.3.1.2 Flash point of Dividend 030 FS

Reference: *Angly, H. 1999c*
Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l
Method: EEC A.9, DIN EN 2719 (Pensky-Marten apparatus)
Results: Negative up to 100 °C (the boiling point of the substance) at 989.0 mbar.
RMS comments: The method used is not sufficiently described. However, since the product is water based, the result is expected to be negative. The method and the result are therefore acceptable.

B.2.2.3.2 Flammability

Not applicable since both formulations are liquids.

B.2.2.3.3 Auto-flammability**B.2.2.3.3.1 Auto-flammability of Score 250 EC**

Reference: *Krips, H. J. 1998e*
Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l
Method: EEC A.15, DIN 51794, IEC 79-4
Results: The lowest auto-ignition temperature was observed to be: 445 °C (100 µl sample was injected).
RMS comments: The method and the result are acceptable.

B.2.2.3.3.1 Auto-flammability of Dividend 030 FS

Reference: *Angly, H. 1998d*
Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l
Method: EEC A.15, DIN 51794
Results: 485 °C when injecting 1.0 ml
RMS comments: The method used is not sufficiently described. However since the formulation is water based auto-flammability is not expected to be a hazard of concern. The method and the result are therefore acceptable.

B.2.2.4 Acidity/alkalinity and pH (Annex IIIA 2.4)

B.2.2.4.1 Acidity/alkalinity (Annex IIIA 2.4.1)

Not applicable, since the pH of a 1% dispersion in water of both preparations are neither lower than 4 nor higher than 10.

B.2.2.4.2 pH of a 1% solution (suspension; Annex IIIA 2.4.2)

B.2.2.4.2.1 pH of a 1% dispersion of Score 250 EC in water

Reference: *Krips, H. J. 1998f*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: CIPAC MT 75.2

Results: pH=6.3 at 20 ± 1 °C

RMS comments: The method and the result are acceptable.

B.2.2.4.2.1 pH of a 1% dispersion of Dividend 030 FS in water

Reference: *Kundel, P. 1999a*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: CIPAC MT 75.2

Results: pH=7.2

RMS comments: The method and the result are acceptable.

B.2.2.5 Viscosity and surface tension (Annex IIIA 2.5)

B.2.2.5.1 Viscosity

B.2.2.5.1.1 Kinematic viscosity (Annex IIIA 2.5.1)

Not required because both preparations are not ultra low volume use products.

B.2.2.5.1.2 Dynamic viscosity (Annex IIIA 2.5.2)

B.2.2.5.1.2.1 Dynamic viscosity of Score 250 EC

Reference: *Krips, H. J. 1998g*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: OECD 114

Results: The viscosity showed a small shear-rate dependency:

at 20 °C the viscosity was determined to be:

min. 35 mPa s at a shear-rate of 224.5 s⁻¹

max. 40 mPa s at a shear-rate of 1220 s⁻¹

at 40 °C the viscosity was determined to be:

min. 13 mPa s at a shear-rate of 696.9 s⁻¹

max. 21 mPa s at a shear-rate of 1227 s⁻¹

RMS comments: The method and the result are acceptable.

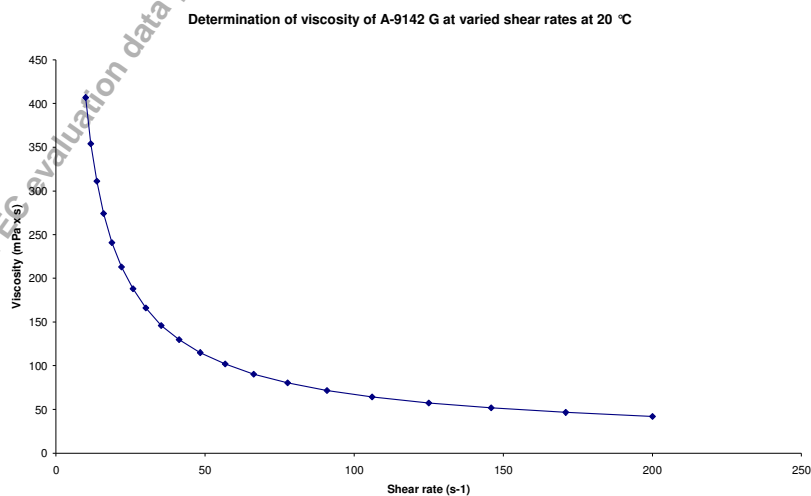
B.2.2.5.1.2.2 Dynamic viscosity of Dividend 030 FS

Reference: *Martin N. 1999a*

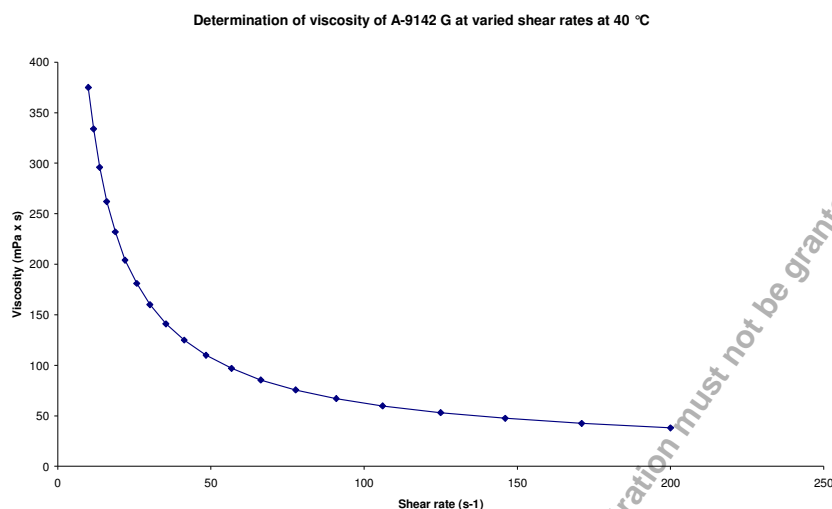
Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: OECD 114 (rotational viscometer)

Results: The preparation was found to be pseudoplastic in its flow behaviour (i.e. it is a non-Newtonian liquid).



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RMS comments: The method and the result are acceptable.

B.2.2.5.2 Surface tension (Annex IIIA 2.5.3)

B.2.2.5.2.1 Surface tension of Score 250 EC

Reference: *Krips, H. J. 1998h*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: EEC A.5

Results: The surface tensions at 20 ± 1 °C was determined to be:

37.7 mN/m for a 0.1% solution (emulsion)

34.2 mN/m for a 1% solution (emulsion)

RMS comments: The method and the results are acceptable.

B.2.2.5.2.2 Surface tension of Dividend 030 FS

Reference: *Martin, N. 1999b*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: EEC A.5, OECD 115, ISO 304

Results: The surface tensions at 20 ± 0.2 °C was determined to be:

38.6 mN/m for a 0.1% solution (emulsion)

34.2 mN/m for a 17% solution (emulsion)

34.6 mN/m for the undiluted material

RMS comments: The method and the results are acceptable.

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B.2.2.6 Relative density and bulk density (Annex IIIA 2.6)

B.2.2.6.1 Relative density (Annex IIIA 2.6.1)

B.2.2.6.1.1 Relative density of Score 250 EC

Reference: *Krips, H. J. 1998b*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: EEC A.3

Results: The density was determined to be:
 $1.059 \times 10^3 \text{ kg/m}^3$ at 20.0 °C

RMS comments: The density is reported instead of the relative density, D_4^{20} which is a dimensionless unit.
As the density of water at 0 °C is 0.9999750 ("Handbook of Chemistry and Physics", 83RD edition, **2002-2003**) the relative density of Score 250 EC is 1.059. Hereby, the method and the result are acceptable.

B.2.2.6.1.2 Relative density of Dividend 030 FS

Reference: *Käser, W. 1999*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: OECD 109 (oscillating density meter)

Results: The density was determined to be:
 $1.049 \times 10^3 \text{ kg/m}^3$

RMS comments: The density is reported instead of the relative density, D_4^{20} which is a dimensionless unit.
Moreover the temperature of the measurement is not reported
As the density of water at 0 °C is 0.9999750 ("Handbook of Chemistry and Physics", 83RD edition, **2002-2003**) the relative density of Dividend 030 FS is 1.049. Hereby, the method and the result are acceptable.

B.2.2.6.2 Bulk (tap) density (Annex IIIA 2.6.2)

Not required because both preparations are liquids.

B.2.2.7 Storage stability and shelf-life (Annex IIIA 2.7)

B.2.2.7.1 Accelerated storage (Annex IIIA 2.7.1)

B.2.2.7.1.1 Accelerated storage of Score 250 EC

Reference: *Krips, H. J. 1998i*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: CIPAC MT 46.1.3 (only the active ingredient content was assessed)

Results: The active ingredient was shown to be stable when stored for 14 days at 54 °C ± 2 °C (initial concentration: 258.3 g/l; after storage: 262.1 g/l).

Reference: *Kundel, P. 1999a*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: GIFAP Mono. 17

Results: The preparation was found to be stable for at least 18 weeks at 30 °C and 80% RH, stored in the sales packaging (fluorinated high-density polyethylene). The test material has been determined to undergo no significant physical or chemical change during the storage as shown in table B.2.2.7.1.1.

Reference: *Kundel, P. 1999b*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: GIFAP Mono. 17

Results: The preparation was found to be stable for at least 18 weeks at 30 °C and 80% RH, stored in the sales packaging (high density polyethylene with an extra barrier of polyamide). The test material has been determined to undergo no significant physical or chemical change during the storage as shown in table B.2.2.7.1.1.

RMS comments: In study 2 and 3 (Kundel, P 1999a-b) all parameters were assessed in accordance with GLP, a part from the appearance and the emulsion properties after storage. This should however not have affected the quality of the results.

In overall all three studies are acceptable and the results show the product to be stable towards accelerated storage.

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Table B.2.2.7.1.1: Chemical and physical properties of A-7402 G (Score 250 EC), initially and after 18 weeks of storage at 30 °C

Test	Results		
	Initial	18 weeks at 30 °C (n fluorinated high density polyethylene pack	18 weeks at 30 °C in high density polyethylene pack with additional barrier material (polyamide)
Active ingredient assay (GC-FID method AF-1044/1): Difenoconazole:	-	250 g/l Reference: 249 g/l	253 g/l Reference: 259 g/l
Density (OECD 109)	1.059 g/cm ³	1.060 g/cm ³	1.059 g/cm ³
Appearance (visual assessment): Formulation:	clear, yellow to brown liquid	clear, yellow to brown liquid	clear, yellow to brown liquid
Container:	-	The packaging is resistant to its content. Weight gain 0.07 %	The packaging is resistant to its content. Weight gain 0.08 %
pH at 20 ± 1 °C (1% dispersion) (CIPAC MT 75.2)	6.3	6.7	6.8
Emulsion properties (CIPAC MT 173): Concentration 0.1% in CIPAC water A Temperature 30 °C Spontaneity of the emulsion:	spontaneous	spontaneous	spontaneous
Stability 30 minutes:	99%, visual homogeneous	99%, visual homogeneous	100%, visual homogeneous
2 hours:	95%, visual homogeneous	95%, visual homogeneous	96%, visual homogeneous
24 hours:	87%, trace cream at bottom	86%, trace cream at bottom (<2 ml)	85%, < 2 ml cream at bottom
Re-emulsification:	complete	complete	complete
Stability after Re-emulsification: Waiting period 30 minutes	100%, visual homogeneous	98%, visual homogeneous	103%, visual homogeneous
Emulsion properties (CIPAC MT 173): Concentration 0.1% in CIPAC water C Temperature 30 °C Spontaneity of the emulsion	spontaneous	spontaneous	spontaneous
Stability 30 minutes	100%, visual homogeneous	100%, visual homogeneous	101%, visual homogeneous
2 hours	99%, visual homogeneous	100%, visual homogeneous	101%, visual homogeneous
24 hours	99%, visual homogeneous	95%, <2 ml cream at bottom	101%, visual homogeneous
Re-emulsification	complete	complete	complete

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Annex B.2: Physical and chemical properties

Test	Results		
	Initial	18 weeks at 30 °C (n fluorinated high density polyethylene pack	18 weeks at 30 °C in high density polyethylene pack with additional barrier material (polyamide)
Stability after Re-emulsification Waiting period 30 minutes	100%, visual homogeneous	100%, visual homogeneous	104%, visual homogeneous
Emulsion properties (CIPAC MT 173): Concentration 1.0% in CIPAC water A Temperature 30 °C Spontaneity of the emulsion	spontaneous	spontaneous	spontaneous
Stability 30 minutes	99%, visual homogeneous	100%, visual homogeneous	100%, visual homogeneous
2 hours	100%, visual homogeneous	100%, visual homogeneous	100%, visual homogeneous
24 hours	84%, < 2 ml cream at bottom	95%, < 2 ml cream at bottom	88%, < 2ml cream at bottom
Re-emulsification	complete	complete	complete
Stability after Re-emulsification Waiting period 30 minutes	100%, visual homogeneous	100%, visual homogeneous	98%, visual homogeneous
Emulsion properties (CIPAC MT 173): Concentration 1.0% in CIPAC water C Temperature 30 °C Spontaneity of the emulsion	spontaneous	spontaneous	spontaneous
Stability 30 minutes	100%, visual homogeneous	99%, visual homogeneous	99%, visual homogeneous
2 hours	100%, visual homogeneous	100%, visual homogeneous	101%, visual homogeneous
24 hours	99%, visual homogeneous	99%, visual homogeneous	104%, visual homogeneous
Re-emulsification	complete	complete	complete
Stability after Re-emulsification Waiting period 30 minutes	100%, visual homogeneous	100%, visual homogeneous	103%, visual homogeneous

B.2.2.7.1.2 Accelerated storage of Dividend 030 FS

Reference: *Kundel, P. 1999b*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: OECD 113

Results: No significant changes in active ingredient content or density were shown after 14 days of

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Annex B.2: Physical and chemical properties

storage at 54 °C ± 2 °C as seen below

Active ingredient content (HPLC)

Reference: 30.8 g/l After storage: 30.9 g/l

Density (OECD 109)

Reference: 1049 kg/m³ After storage: 1049 kg/m³

Reference: *Kundel, P. 1999c*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: GIFAP Mono. 17

Results: The preparation was found to be stable for at least 18 weeks at 30 °C, stored in the sales packaging (high density polyethylene). The test material has been determined to undergo no significant physical or chemical change during the storage as shown in table B.2.2.7.1.2.

Reference: *Kundel, P. 1999d*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: GIFAP Mono. 17

Results: The preparation was found to be stable for at least 18 weeks at 30 °C, stored in the sales packaging (steel drums with inner varnish). The test material has been determined to undergo no significant physical or chemical change during the storage as shown in table B.2.2.7.1.2.

RMS comments: In study 2 and 3 (Kundel, P. 1999c-d) only the pH and the density were determined in accordance with GLP. This should however not have affected the quality of the results. In overall all three studies are acceptable and the results show the product to be stable towards accelerated storage.

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Annex B.2: Physical and chemical properties

Table B.2.2.7.1.2: Chemical and physical properties of A-9142 G (Dividend 030 FS), initially and after 18 weeks of storage at 30 °C

Test	Results		
	Initial	18 weeks at 30 °C in high density polyethylene pack	18 weeks at 30 °C in steel drum with inner varnish
Active ingredient assay (HPLC method AF-1385/ 1): Difenoconazole:	-	31.3 g/l Reference: 31.3 g/l	30.9 g/l Reference: 31.1 g/l
Density (OECD 109)	1.049 g/cm ³	1.049 g/cm ³	1.049 g/m ³
Appearance (visual assessment): Formulation: Container:	red liquid -	red liquid The packaging is resistant to its content. No permeation through walls Weight loss 0.01 %	red liquid The packaging is resistant to its content. No weight change
Odour (organoleptic)	sweetish, chalky	sweetish, chalky	sweetish, chalky
pH at 20 ± 1 °C (1% dispersion) (CIPAC MT 75.2)	7.2	7.0	7.1
Wet sieve test (CIPAC MT 59.3) sieve mesh size 75 µm	<0.01 %	<0.01 %	0.01%
Persistent Foam (CIPAC MT 47.2) Conc.: 17% in CIPAC water D waiting period 1 min	1 ml	0 ml	0 ml
Pourability (CIPAC MT 148) pour residue: rinsed residue:	3.3% 0.4%	3.6% 0.4%	3.1% 0.3%

B.2.2.7.2 Storage at low temperature (Annex IIIA 2.7.2)

B.2.2.7.2.1 Storage at low temperature of Score 250 EC

Reference: *Krips, H. J. 1998j*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: CIPAC MT 39.1

Results: After 7 days of incubation period at 0.0 ± 1 °C, a trace of white sediment was observed at the bottom of the sample. However the product was considered to be stable since no significant changes in the test material consistency have occurred.

RMS comments: The method and the results are acceptable.

B.2.2.7.2.2 Storage at low temperature of Dividend 030 FS

Reference: *Kalt, R. 1999b*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: CIPAC MT 39.1. In addition at the end of the storage period a wet sieving (CIPAC MT 59.3) was performed to further assess the stability.

Results: After 7 days of incubation period at 0.0 ± 1 °C, no separation was observed. In the wet sieving a residue of 0.01% was retained on the 75 µm sieve.

RMS comments: The product is considered to be stable towards low temperature storage.

The study is not performed in accordance with GLP. The method and the results are still acceptable.

B.2.2.7.3 Shelf life (Annex IIIA 2.7.3)

B.2.2.7.3.1 Shelf life of Score 250 EC

Reference: *Kundel, P. 2000a*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: GIFAP Mono. 17 (stated in summary document MIII, section 1)

Results: The test material has been determined to undergo no significant physical or chemical change when stored in the sales packaging (fluorinated high-density polyethylene) at ambient (20 °C; 50% RH), as shown in table B.2.2.7.3.1. The shelf-life is at least two years.

Reference: *Kundel, P. 2000b*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: GIFAP Mono. 17 (stated in summary document MIII, section 1)

Results: The test material has been determined to undergo no significant physical or chemical change when stored in the sales packaging (high density polyethylene with additional barrier material of polyamide) at ambient (20 °C; 50% RH), as shown in table B.2.2.7.3.1. The shelf-life is at least two years.

RMS comments: In both studies all initial measurements were performed in accordance with GLP. However, after storage only the assessment of pH, density and the active ingredient content were performed in accordance with GLP. This should not have affected the quality of the results. The method and the results are therefore acceptable.

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Table B.2.2.7.3.1: Chemical and physical properties of A-7402 G (Score 250 EC), initially and after 2 years storage at ambient.

Test	Results		
	Initial	2 years at ambient temperature in fluorinated high density polyethylene pack	2 years at ambient temperature in high density polyethylene pack with additional barrier material (polyamide)
Active ingredient assay (GC-FID method AF-1044/1): Difenoconazole:	-	256 g/l Reference: 256 g/l	254 g/l Reference: 256 g/l
Density (OECD 109)	1.059 g/cm ³	1.055 g/cm ³	1.055 g/cm ³
Appearance (visual assessment): Formulation:	clear, yellow to brown liquid	clear, yellow to brown liquid	clear, yellow to brown liquid
Container:	-	The packaging is resistant to its content. No permeation through walls Weight gain 0.12%	The packaging is resistant to its content. No permeation through walls Weight gain 0.11%
Odour (organoleptic)	penetrating	penetrating	penetrating
pH at 20 ± 1 °C (1% dispersion) (CIPAC MT 75.2)	6.3	6.5	6.6
Persistent foam (CIPAC MT 47.2) waiting period 1 min:	14 ml	12 ml	18 ml
Emulsion properties (CIPAC MT 173): Concentration 0.1% in CIPAC water A Temperature 30 °C Spontaneity of the emulsion:	spontaneous	spontaneous	spontaneous
Stability 30 minutes:	99%, visual homogeneous	97%, visual homogeneous	99%, visual homogeneous
2 hours:	95%, visual homogeneous	99%, trace cream at bottom	96%, trace cream at bottom
24 hours:	87%, trace cream at bottom	84%, trace cream at bottom	78%, trace cream at bottom
Re-emulsification:	complete	complete	complete
Stability after Re-emulsification: Waiting period 30 minutes	100%, visual homogeneous	94%, visual homogeneous	98%, visual homogeneous
Emulsion properties (CIPAC MT 173): Concentration 0.1% in CIPAC water C Temperature 30 °C Spontaneity of the emulsion:	spontaneous	spontaneous	spontaneous
Stability 30 minutes:	100%, visual homogeneous	100%, visual homogeneous	99%, visual homogeneous
2 hours:	99%, visual homogeneous	100%, visual homogeneous	99%, visual homogeneous

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Test	Results		
	Initial	2 years at ambient temperature in fluorinated high density polyethylene pack	2 years at ambient temperature in high density polyethylene pack with additional barrier material (polyamide)
24 hours:	99%, visual homogeneous	98%, visual homogeneous	97%, visual homogeneous
Re-emulsification:	complete	complete	complete
Stability after Re-emulsification: Waiting period 30 minutes	100%, visual homogenous	97%, visual homogeneous	97%, visual homogeneous
Emulsion properties (CIPAC MT 173): Concentration 1.0% in CIPAC water A Temperature 30 °C Spontaneity of the emulsion:	spontaneous	spontaneous	spontaneous
Stability 30 minutes:	99%, visual homogeneous	98%, visual homogeneous	100%, visual homogeneous
2 hours:	100%, visual homogeneous	100%, trace cream at bottom	100%, trace cream at bottom
24 hours:	84%, < 2 ml cream at bottom	89%, trace cream at bottom	89%, trace cream at bottom
Re-emulsification:	complete	complete	complete
Stability after Re-emulsification: Waiting period 30 minutes	100%, visual homogeneous	98%, visual homogeneous	97%, visual homogeneous
Emulsion properties (CIPAC MT 173): Concentration 1.0% in CIPAC water C Temperature 30 °C Spontaneity of the emulsion:	spontaneous	spontaneous	spontaneous
Stability 30 minutes:	100%, visual homogeneous	99%, visual homogeneous	99%, visual homogeneous
2 hours:	100%, visual homogeneous	101%, visual homogeneous	100%, visual homogeneous
24 hours:	99%, visual homogenous	100%, visual homogeneous	99%, visual homogeneous
Re-emulsification:	complete	complete	complete
Stability after Re-emulsification: Waiting period 30 minutes	100%, visual homogenous	97%, visual homogeneous	103%, visual homogeneous

B.2.2.7.3.2 Shelf life of Dividend 030 FS

Reference: *Kundel, P. 2001a*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: GIFAP Mono. 17 (stated in summary document MIII, section 1)

Results: The test material has been determined to undergo no significant physical or chemical change when stored in the sales packaging (high density polyethylene) at ambient (20 °C), as shown in table B.2.2.7.3.2. The shelf-life is at least two years.

RMS comments: In both studies only the pH and the density were determined in accordance with GLP. This should however not have affected the quality of the results.
The method and the results are therefore acceptable.

Reference: *Kundel, P. 2001b*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: GIFAP Mono. 17 (stated in summary document MIII, section 1)

Results: The test material has been determined to undergo no significant physical or chemical change when stored in the sales packaging (steel drums with inner varnish) at ambient (20 °C), as shown in table B.2.2.7.3.2. The shelf-life is at least two years.

RMS comments: In both studies only the pH and the density were determined in accordance with GLP. This should however not have affected the quality of the results.
The method and the results are therefore acceptable.

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Table B.2.2.7.3.2: Chemical and physical properties of A-9142 G (Dividend 030 FS), initially and after 2 years storage at ambient.

Test	Results		
	Initial	2 years at ambient temperature in high density polyethylene pack	2 years at ambient temperature in steel drum with inner varnish
Active ingredient assay (HPLC method AF-1385/ 1): Difenoconazole:	-	30.9 g/l Reference: 30.9 g/l	30.9 g/l Reference: 30.7 g/l
Density (OECD 109)	1.049 g/cm ³	1.049 g/cm ³	1.049 g/m ³
Appearance (visual assessment): Formulation: Container:	red liquid -	red liquid The packaging is resistant to its content. No permeation through walls. Weight loss 0.07 %	red liquid The packaging is resistant to its content. Weight loss 0.01 %
Odour (organoleptic)	sweetish, chalky	sweetish, chalky	sweetish, chalky
pH at 20 ± 1 °C (1% dispersion) (CIPAC MT 75.2)	7.2	7.0	7.1
Wet sieve test (CIPAC MT 59.3) sieve mesh size 75 µm	< 0.01 %	< 0.01 %	0.01 %
Persistent Foam (CIPAC MT 47.2) Conc.: 17% in CIPAC water D waiting period 1 min	1 ml	0 ml	0 ml
Pourability (CIPAC MT 148) pour residue: rinsed residue:	3.3% 0.4%	2.6% 0.3%	2.6% 0.2%

B.2.2.8 Technical characteristics (Annex IIIA 2.8)

B.2.2.8.1 Wettability (Annex IIIA 2.8.1)

Not required since both preparations are liquids.

B.2.2.8.2 Persistent foaming (Annex IIIA 2.8.2)

B.2.2.8.2.1 Persistent foaming of Score 250 EC

Reference: *Krips, H. 1998j*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: CIPAC MT 47.2 (1% v/v suspension)

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Results:

Time	Volume of foam (ml)
10 seconds	16
1 minute	14
3 minutes	14
12 minutes	12

RMS comments: The method and the result are acceptable.

B.2.2.8.2.2 Persistent foaming of Dividend 030 FSReference: *Kalt, R. 1999a*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: CIPAC MT 47.2 (17% v/v suspension)

Results:

Time	Volume of foam (ml)
10 seconds	54
1 minute	1
3 minutes	0
12 minutes	0

RMS comments: The test is not performed in accordance with GLP. This should however not have affected the quality of the result. The method is therefore acceptable.

B.2.2.8.3 Suspensibility and Suspension stability (Annex IIIA 2.8.3)**B.2.2.8.3.1 Suspensibility and Suspension stability of Score 250 EC**

Not applicable to a emulsion concentrate

B.2.2.8.3.2 Suspensibility and Suspension stability of Dividend 250 ECReference: *Kalt, R. 1999b*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method:

1. CIPAC MT 161
2. CIPAC MT 160

Results:

1. 30 min: 100% (17% v/v suspension)
2. 98%

RMS comments: The study was not performed in accordance with GLP.
The methods and the results are still acceptable.

B.2.2.8.4 Dilution stability (Annex IIIA 2.8.4)

Not required because the preparations are not water soluble.

B.2.2.8.5 Dry sieve test and wet sieve test (Annex IIIA 2.8.5)**B.2.2.8.5.1 Dry sieve test**

Not applicable, since the formulations are not dustable powder.

B.2.2.8.5.2 Wet sieve test**B.2.2.8.5.2.1 Wet sieve test for Score 250 EC**

Not applicable since the formulation is not water dispersible.

B.2.2.8.5.2.2 Wet sieve test for Dividend 030 FS

Reference: *Kalt, R. 1999a-b*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: CIPAC MT 59.3

Results: <0.01% (75 µm sieve)

RMS comments: The test is not performed in accordance with GLP. This should however not have affected the quality of the result. The method is therefore acceptable.

B.2.2.8.6 Particle size distribution, content of dust/fines, attrition and friability (Annex IIIA 2.8.6)**B.2.2.8.6.1 Particle size distribution (Annex IIIA 2.8.6.1)**

Not required because both preparations are liquid.

B.2.2.8.6.2 Content of dust/fines (Annex IIIA 2.8.6.2)

Not required because both preparations are liquid.

B.2.2.8.6.3 Friability and attrition characteristics of granules (Annex IIIA 2.8.6.3)

Not required because both preparations are liquid.

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B.2.2.8.7 Emulsifiability, re-emulsifiability and emulsion stability (Annex IIIA 2.8.7)

B.2.2.8.7.1 Emulsifiability, re-emulsifiability and emulsion stability of Score 250 EC

Reference: *Krips, H.J 1998f*

Test Material: A-7402 G, Batch No.: P.612076, concentration of active substance: 259 g/l

Method: CIPAC MT 173

Results: See table B.2.2.8.7.1 below.

RMS comments: The method and the results are acceptable.

Table B.2.2.8.7.1: Emulsifiability, re-emulsifiability and emulsion stability of A-7402 G (Score 250 EC)

Properties	Results			
	Cond. 1	Cond. 2	Cond. 3	Cond. 4
Spontaneity:	spontaneous	spontaneous	spontaneous	spontaneous
Stability:				
After 0.5 h	99%, visual homogeneous	100%, visual homogeneous	99%, visual homogeneous	100%, visual homogeneous
After 2 h	100%, visual homogeneous	100%, visual homogeneous	95%, visual homogeneous	99%, visual homogeneous
After 24 h	84%, cream at bottom (<2ml)	99%, visual homogeneous	87%, trace cream at the bottom	99%, visual homogeneous
Re-emulsification:				
Stability after 0.5 h:	complete 100%, visual homogeneous	complete 100%, visual homogeneous	complete 100%, visual homogeneous	complete 100%, visual homogeneous

Cond. 1.: Conc. 1.0%, temp 30 °C, CIPAC water A

Cond. 2.: Conc. 1.0%, temp 30 °C, CIPAC water C

Cond. 3.: Conc. 0.1%, temp 30 °C, CIPAC water A

Cond. 3.: Conc. 0.1%, temp 30 °C, CIPAC water C

B.2.2.8.7.2 Emulsifiability, re-emulsifiability and emulsion stability of Dividend 030 FS

Not applicable, since it is not an emulsifiable preparation.

B.2.2.8.8 Flowability, pourability and dustability (Annex IIIA 2.8.8)

B.2.2.8.8.1 Flowability (Annex IIIA 2.8.8.1)

Not required because the preparations are not granular formulations

B.2.2.8.8.2 Pourability (Annex IIIA 2.8.8.2)**B.2.2.8.8.2.1 Pourability of Score 250 EC**

Not applicable to emulsion preparations

B.2.2.8.8.2.2 Pourability of Dividend 030 FS

Reference: *Kalt, R. 1999a*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: CIPAC MT 148

Results: Pour residue, R=3.3%

Rinsed residue, R'=0.4%

RMS comments: The test is not performed in accordance with GLP. This should however not have affected the quality of the result. The method is therefore acceptable.

B.2.2.8.8.3 Dustability (Annex IIIA 2.8.8.3)

Not required because the preparations are not dustable powders.

B.2.2.9 Physical and chemical compatibility with other products (Annex IIIA 2.9)

No application is being made for the authorisation of the combined use of the preparations with any other product.

B.2.2.10 Adherence and distribution to seeds (Annex IIIA 2.10)**B.2.2.10.1 Adherence and distribution to seeds of Score 250 EC**

Not required because the preparation is not for seed treatment.

B.2.2.10.2 Adherence and distribution to seeds for Dividend 030 FS

Reference: *Kalt, R. 1999c*

Test Material: A-9142 G, Batch No.: P.902001, concentration of active substance: 30.6 g/l

Method: CIPAC MT 175

Results: Average absorption value: 0.134

Standard deviation: 0.024

Minimum value: 0.091

Maximum value: 0.223

Thousand grain weight: 45.53 g

RMS comments: The method and the results are acceptable.

B.2.2.11 Summary and evaluation of data presented under points B.2.2.1 - B.2.2.10 (Annex IIIA 2.11)

Data for two representative formulations, Score 250 EC and Dividend 030 FS was submitted:

Score 250 EC

All tests on the physical and chemical properties of Score 250 EC have been performed with the obsolete formulation A-7402 G. However this procedure is acceptable since A-7402 G and the representative formulation A-7402 T (Score 250 EC) are considered equivalent regarding the physical and chemical properties (see Annex C for further details).

Study reports with regard to physical and chemical properties of the preparation have been submitted for all relevant parameters.

The tests have been performed according to the methods recommended in Annex III of the directive 91/414/EEC, except the oxidizing properties, which was assessed in accordance with the Recommendation on the Transport of Dangerous Goods, Manual of Test and Criteria. Part III, section 34. United Nations, 1995. Furthermore, all of the tests have been performed in accordance with GLP, except some studies performed in connection with the storage stability studies. All the tests and the methods used are considered acceptable.

Score 250 EC (A-7402 T) is a clear yellow to brown liquid emulsion concentrate formulation with a penetrating odour. The formulation is not oxidizing or explosive and has an auto-ignition temperature of 445 °C. pH of a 1% suspension of the formulation is 6.3. The formulation was proven to be stable in accelerated storage tests for at least 2 weeks at 54 °C and for at least 18 weeks at 30 °C, when kept in the sales packaging. Moreover, the shelf life of the product at ambient temperature, when kept in the sales packaging, was proved to be at least two years. All other physical and chemical properties indicate that no particular problems are to be expected when used and stored as recommended on the label. The physical-chemicals properties of Score 250 EC are summarized in table B.2.2.11-1.

Dividend 030 FS

Study reports with regard to physical and chemical properties of the preparation have been submitted for all relevant parameters.

The tests have been performed according to the methods recommended in Annex III of the directive 91/414/EEC, except the oxidizing properties, which was assessed in accordance with the Recommendation on the Transport of Dangerous Goods, Manual of Test and Criteria. Part III, section 34. United Nations, 1995. Furthermore, most of the tests have been performed in accordance with GLP except the appearance, some assessments performed in connection with the storage stability studies, the persistent foaming, the suspensibility, the wet sieve test and the pourability. All the tests and the methods used are considered acceptable.

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Dividend 030 FS (A-9142 G) is a red flowable concentrate for seed treatment with a sweetish, chalky odour. The formulation is not oxidizing or explosive and has an auto-ignition temperature of 485 °C. pH of a 1% suspension of the formulation is 7.2. When the viscosity was tested Dividend 030 FS was shown to be pseudoplastic in its flow behaviour (i.e it is a non-Newtonian liquid). The formulation was proven to be stable in accelerated storage tests for at least 2 weeks at 54 °C and for at least 18 weeks at 30 °C when kept in the sales packaging. Moreover, the shelf life of the product at ambient temperature, when kept in the sales packaging, was proved to be at least two years. All other physical and chemical properties indicate that no particular problems are to be expected when used and stored as recommended on the label. The physical-chemicals properties of Dividend 030 FS are summarized in table B.2.2.11-2.

Table B.2.2.11-1: Summary of the physical and chemical properties of Score 250 EC-(difenoconazole 250 g/l-EC)

Identity, Physical and Chemical Properties	Results	Study Document Available	EEC method or equivalent	GLP	Comments
Product name	Score 250 EC				
Product code number	A-7402 T (the older formulation A-7402 G has been used in the tests on physical and chemical properties; see document C for further details.)				
Concentration of active ingredient	250 g/l				
Physical state and appearance at room temperature	Clear yellow to brown liquid	Y	visual observation	Y	
Odour	Penetrating	Y	Organoleptic	Y	
Explosive properties	Not explosive	Y	EEC A.14	Y	
Oxidizing properties	The preparation is not an oxidizer	Y	Recommendation on the Transport of Dangerous Goods, Manual of Test and Criteria. Part III, section 34. United Nations, 1995	Y	
Flash point, °C, 101.3 kPa	63 °C	Y	EEC A.9	Y	
Flammability	Not applicable				
Auto-flammability	445 °C	Y	EEC A.15, DIN 51794, IEC 79-4	Y	
Acidity/alkalinity	Not applicable				
pH of a 1 % solution, (dispersion in water)	6.3	Y	CIPAC MT 75.2	Y	
Kinematic viscosity	Not for ULV use				
Dynamic viscosity, mPa/s	<u>20 °C</u> min. 35 mPa s at a shear-rate of 224.5 s ⁻¹ max. 40 mPa at a shear-rate of 1220 s ⁻¹ <u>40 °C</u> min. 13 mPa s at a shear-rate of 696.9 s ⁻¹ max. 21 mPa at a shear-rate of 1227 s ⁻¹	Y	OECD 114	Y	

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Identity, Physical and Chemical Properties	Results	Study Document Available	EEC method or equivalent	GLP	Comments
Surface tension, mN/m, at 20 °C	$\sigma=37.7$ mN/m (0.1% v/v aqueous emulsion) $\sigma=34.2$ mN/m (1% v/v aqueous emulsion)	Y	EEC A.5	Y	
Relative density, D_4^{20}	1.059×10^3 kg/m ³ at 20 °C	Y	EEC A.3	Y	The density is reported. Relative density is 1.059
Bulk (tap) density	Not applicable				
Storage stability at 54°C for 14 days	The preparation underwent no significant changes in content of active material and in the physical properties.	Y	CIPAC MT 46.1.3,	Y	
Storage stability at 30 °C for 18 weeks in the sales packaging	The preparation underwent no significant changes in content of active material and in the physical properties.	Y	GIFAP Mono. 17	N	All initial studies were performed in accordance with GLP. Some of the post-storage analyses were performed according to GLP.
Storage stability at low temperature	Stable	Y	CIPAC MT 39.1	Y	
Shelf life at ambient temperature	At least 2 years at room temperature if stored in the sales packing since the preparation underwent no significant changes in content of active material and in the physical properties.	Y	GIFAP Mono. 17	N	All initial studies were performed in accordance with GLP. Some of the post-storage analyses were performed according to GLP.
Wettability	Not applicable				
Persistent foaming	16 ml after 10 seconds 14 ml after 1 minute 14 ml after 3 minutes 12 ml after 12 minutes	Y	CIPAC MT 47.2	Y	
Suspensibility and suspension stability	Not applicable				
Dilution stability	Not applicable				
Dry sieve test	Not applicable				
Wet sieve test	Not applicable				
Particle size distribution	Not applicable				
Content of dust/fines	Not applicable				
Friability and attrition characteristics of granules	Not applicable				
Emulsifiability, re-emulsifiability, emulsion stability and stability of dilute emulsions	The product has acceptable emulsion properties as shown in table B.2.2.8.7.1	Y	CIPAC MT 173	Y	
Flowability	Not applicable				
Pourability	Not applicable				
Dustability	Not applicable				
Physical compatibility of tank mixes	Not applicable				
Chemical compatibility of tank mixes	Not applicable				
Adherence and distribution to seeds	Not applicable				

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Table B.2.2.11-2: Summary of the physical and chemical properties of Dividend 030 FS-(difenoconazole 30 g/l-FS)

Identity, Physical and Chemical Properties	Results	Study Document Available	EEC method or equivalent	GLP	Comments
Product name	Dividend 030 FS				
Product code number	A-9142 G				
Concentration of active ingredient	30 g/l				
Physical state and appearance at room temperature	red liquid	Y	visual observation	N	
Odour	sweetish, chalky	Y	organoleptic	N	
Explosive properties	not explosive	Y	EEC A.14	Y	
Oxidizing properties	the preparation is not an oxidizer	Y	Recommendation on the Transport of Dangerous Goods, Manual of Test and Criteria. Part III, section 34. United Nations, 1995	Y	
Flash point, °C, 101.3 kPa	Negative up to 100 °C (the boiling point)	Y	EEC A.9	Y	
Flammability	Not applicable				
Auto-flammability	485 °C	Y	EEC A.15, DIN 51794,	Y	
Acidity/alkalinity	Not applicable				
pH of a 1% solution, (dispersion in water)	7.2	Y	CIPAC MT 75.2	Y	
Kinematic viscosity	Not for ULV use				
Dynamic viscosity, mPa/s	Pseudoplastic flow behaviour. Flow curves are presented.	Y	OECD 114	Y	
Surface tension, mN/m, at 20 °C	σ=38.6 mN/m (0.1% v/v aqueous emulsion) σ=34.2 mN/m (17% v/v aqueous emulsion) σ=34.6 mN/m (undiluted material)	Y	EEC A.5, OECD 115, ISO 304	Y	
Relative density, D_4^{20}	1.049 x 10 ³ kg/m ³ at 20 °C	Y	OECD 109	Y	The density is reported. Relative density is 1.049
Bulk (tap) density	Not applicable				
Storage stability at 54°C for 14 days	The preparation underwent no significant changes in content of active material and in the physical properties.	Y	OECD 113	Y	
Storage stability at 30 °C for 18 weeks in the sales packaging	The preparation underwent no significant changes in content of active material and in the physical properties.	Y	GIFAP Mono. 17	N	Only the pH and the density were assessed in accordance with GLP.
Storage stability at low temperature	Stable	Y	CIPAC MT 39.1	N	

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Identity, Physical and Chemical Properties	Results	Study Document Available	EEC method or equivalent	GLP	Comments
Shelf life at ambient temperature	At least 2 years at room temperature if stored in the sales packing since the preparation underwent no significant changes in content of active material and in the physical properties.	Y	GIFAP Mono. 17	N	Only pH, the density and the active ingredient content (pre- and post-storage) were determined in accordance with GLP.
Wettability	Not applicable				
Persistent foaming	54 ml after 10 seconds 1 ml after 1 minute 0 ml after 3 minutes 0 ml after 12 minutes	Y	CIPAC MT 47.2	N	
Suspensibility and suspension stability	<u>suspensibility</u> : 30 min: 100% (17% v/v suspension) <u>spontaneity</u> : 98%	Y	CIPAC MT 161, CIPAC MT 160	N	
Dilution stability	Not applicable				
Dry sieve test	Not applicable				
Wet sieve test	<0.01% (75 µm sieve)	Y	CIPAC MT 59.3	N	
Particle size distribution	Not applicable				
Content of dust/fines	Not applicable				
Friability and attrition characteristics of granules	Not applicable				
Emulsifiability, re-emulsifiability, emulsion stability and stability of dilute emulsions	Not applicable				
Flowability	Not applicable				
Pourability	Pour residue: 3.3% Rinsed residue: 0.40%	Y	CIPAC MT 148	N	
Dustability	Not applicable				
Physical compatibility of tank mixes	Not applicable				
Chemical compatibility of tank mixes	Not applicable				
Adherence and distribution to seeds	Average absorption value: 0.134 Standard deviation: 0.024 Minimum value: 0.091 Maximum value: 0.223 Thousand grain weight: 45.53 g	Y	CIPAC MT 175	Y	

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B.2.3 References relied on

Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N*	Owner [†]
IIA 2.1.1/01	Das, R.	1999a	Report on melting point / melting range Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland, Report No 70157 GLP Not Published Syngenta File N° CGA169374/1686	N	SYN
IIA 2.1.2/01 IIA 2.1.3/01	Das, R.	1997	Report on boiling point / boiling range Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland, Report No 54326 GLP Not Published Syngenta File N° CGA169374/1462	N	SYN
IIA 2.1.3/02	Schürch, H.	1993	Report on thermal stability and stability in the air Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No PP-93-16T-TSA GLP Not Published Syngenta File N° CGA169374/0808	N	SYN
IIA 2.2/01	Földner, H.H.	1999	Report on density of solids Novartis Crop Protection AG, Basel, Switzerland Novartis Services AG, Basel, Switzerland, Report No PP-98/137P.DES GLP Not Published Syngenta File N° CGA169374/1829	N	SYN
IIA 2.3.1/01	Rordorf, B.	1988	Report on vapor pressure curve Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No AG-88-11P GLP Not Published Syngenta File N° CGA169374/0690	N	SYN
IIA 2.3.1/02	Krohn, J.	2001a	Vapour pressure curve of 1,2,4-triazole Syngenta Crop Protection AG, Basel, Switzerland Bayer AG, Leverkusen, Germany, Report No 100415 Not GLP Not Published Syngenta File N° CGA71019/0049	N	SYN

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Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N*	Owner [†]
IIA 2.3.1/03	Widmer, H.	2001a	Vapour pressure of CGA 205375 Syngenta Crop Protection AG, Basel, Switzerland, Report No 2001WI07 GLP Not Published Syngenta File N° CGA205375/0006	N	SYN
IIA 2.3.2/01	Burkhard, N.	1998	Henry's law constant Brian Christensen Companies, Inc., Minnetonka, United States Novartis Crop Protection AG, Basel, Switzerland, Report No N/A Syngenta File N° CGA169374/0785	N	SYN
IIA 2.4.1/01 IIA 2.4.2/01	Das, R.	1999b	Report on general physico-chemical properties (pure active ingredient - colour, aspect and odour) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland, Report No 70160 GLP Not Published Syngenta File N° CGA169374/1685	N	SYN
IIA 2.4.1/02 IIA 2.4.2/02	Das, R.	1993	Report on general physico-chemical properties Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Mönchwil AG, Mönchwil, Switzerland, Report No 8804 GLP Not Published Syngenta File N° CGA169374/0756	N	SYN
IIA 2.5.1/01	Oggenfuss, P.	1999	Spectra of CGA 169374 Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland, Report No 77913 GLP Not Published Syngenta File N° CGA169374/1948	N	SYN
IIA 2.6/01	Stulz, J.	1994	Report on water solubility Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Mönchwil AG, Mönchwil, Switzerland, Report No 23321 GLP Not Published Syngenta File N° CGA169374/0688	N	SYN
IIA 2.6/02	Krohn, J.	2001b	Water solubility and Henry law constant of 1,2,4-triazole Syngenta Crop Protection AG, Basel, Switzerland Bayer AG, Leverkusen, Germany, Report No MO-01-005554 Not GLP Not Published Syngenta File N° CGA71019/0050	N	SYN

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DIFENOCONAZOLE
Annex B.2: Physical and chemical properties

Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N*	Owner [†]
IIA 2.6/03	Das, R.	2001a	Water solubility of CGA 205375 Syngenta Crop Protection AG, Basel, Switzerland Syngenta Crop Protection Munchwilen AG, Munchwilen, Switzerland, Report No 107459 GLP Not Published Syngenta File N° CGA205375/0007	N	SYN
IIA 2.7/01	Kettner, R.	1999a	Solubility in organic solvents of CGA 169374 Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Munchwilen AG, Munchwilen, Switzerland, Report No 76994 GLP Not Published Syngenta File N° CGA169374/1958	N	SYN
IIA 2.8/01	Kettner, R.	1999b	Octanol / water partition coefficient of CGA 169374 Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Munchwilen AG, Munchwilen, Switzerland, Report No 76303 GLP Not Published Syngenta File N° CGA169374/1915	N	SYN
IIA 2.8/02	Widmer, H	2005	Determination of the Partition Co-efficient [N-Octanol/Water] of CGA71019 including effect of pH. RCC Ltd Environmental Chemistry and Pharmanalytics, Switzerland Report No. A31612 Not published GLP Syngenta File No. CGA71019/0091	Y	SYN
IIA 2.8/03	Das, R.	2001b	Octanol / water partition coefficient of CGA 205375 Syngenta Crop Protection AG, Basel, Switzerland Syngenta Crop Protection Munchwilen AG, Munchwilen, Switzerland, Report No 107458 GLP Not Published Syngenta File N° CGA205375/0005	N	SYN
IIA 2.9.1/01	Atkins, R.H.	1991	Hydrolysis of 14C CGA169374 at pH 5, 7 and 9 Novartis Crop Protection AG, Basel, Switzerland PTRL East, Inc., Richmond, United States, Report No 494 GLP Not Published Syngenta File N° CGA169374/0488	N	SYN

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IIA 2.9.2/01	Van, der Gaauw A.	2002	Aqueous Photolysis of CGA169374 [14C-Triazole] under Laboratory Conditions Syngenta Crop Protection AG, Basel, Switzerland RCC Ltd., Itingen, Switzerland, Report No 815635 GLP Not Published Syngenta File N° CGA169374/2209	Y	SYN
IIA 2.9.3/01	Hennecke, D.	2002	Quantum Yield of the photochemical degradation of CGA169374 in aqueous solution Syngenta Crop Protection AG, Basel, Switzerland Fraunhofer Institut für Umweltchemie und Oekotoxikologie, Schmallenberg, Germany, Report No SYN-001/7-05 GLP Not Published Syngenta File N° CGA169374/2208	Y	SYN
IIA 2.9.4/01	Hörmann, A.	1999	Final report on dissociation constant in water Novartis Crop Protection AG, Basel, Switzerland Novartis Services AG, Basel, Switzerland, Report No 70159 GLP Not Published Syngenta File N° CGA169374/1817	N	SYN
IIA 2.10/01	Stamm, E.	1998	Atmospheric oxidation of Difenconazole CGA 169374 by hydroxyl radicals; rate estimation Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection AG, Basel, Switzerland, Report No 98SM18 Not GLP Not Published Syngenta File N° CGA169374/1669	N	SYN
IIA 2.11.1/01	Schürch, H.	1992a	Report on flammability of solids Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No AG 91/14T.FLS GLP Not Published Syngenta File N° CGA169374/0687	N	SYN
IIA 2.11.2/01	Schürch, H.	1992b	Report on autoflammability of solids Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No AG 91/14T.AFS GLP Not Published Syngenta File N° CGA169374/0686	N	SYN

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IIA 2.13/01	Schürch, H.	1992c	Report on explosive properties Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No AG 91/14T.EXP GLP Not Published Syngenta File N° CGA169374/0685	N	SYN
IIA 2.14/01	Martin, N.	1999	Surface tension Novartis Crop Protection AG, Basel, Switzerland Solvias AG, Basel, Switzerland, Report No PP 99/79T.SUR GLP Not Published Syngenta File N° CGA169374/1982	N	SYN
IIA 2.15/01	Schürch, H.	1992d	Report on oxidizing properties Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No AG 91/14T.OXP GLP Not Published Syngenta File N° CGA169374/0684	N	SYN
IIIA1 2.2.1/01	Krips, H.J.	1998c	Report on determination of the explosive properties Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235777 GLP Not Published Syngenta File N° CGA169374/1871	N	SYN
IIIA2 2.2.1/01	Angly, H.	1999a	Report on explosive properties Novartis Crop Protection AG, Basel, Switzerland Institute of Safety and Security, Basel, Switzerland Report No 1999.4023.EXP GLP, Not Published Syngenta File N° CGA169374/1788	N	SYN
IIIA1 2.2.2/01	Angly, H.	1999	Report on oxidizing properties (liquids) Novartis Crop Protection AG, Basel, Switzerland Institute of Safety and Security, Basel, Switzerland, Report No 1999.4080.OPL GLP Not Published Syngenta File N° CGA169374/1993	N	SYN
IIIA2 2.2.2/01	Angly, H.	1999b	Report on oxidizing properties (liquids) Novartis Crop Protection AG, Basel, Switzerland Institute of Safety and Security, Basel, Switzerland Report No 1999.4023.OPL GLP, Not Published Syngenta File N° CGA169374/1786	N	SYN

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IIIA1 2.3.1/01	Krips, H.J.	1998d	Report on determination of the flash point Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235788 GLP Not Published Syngenta File N° CGA169374/1872	N	SYN
IIIA2 2.3.1/01	Angly, H.	1999c	Report on determination of flash-point Novartis Crop Protection AG, Basel, Switzerland Institute of Safety and Security, Basel, Switzerland Report No 1999.4023.FLP GLP, Not Published Syngenta File N° CGA169374/1787	N	SYN
IIIA1 2.3.3/01	Krips, H.J.	1998e	Report on determination of the auto-ignition temperature (liquids) Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235799 GLP Not Published Syngenta File N° CGA169374/1870	N	SYN
IIIA2 2.3.3/01	Angly, H.	1999d	Report on auto-ignition temperatur (liquid and gases) Novartis Crop Protection AG, Basel, Switzerland Institute of Safety and Security, Basel, Switzerland Report No 1999.4023.AFG GLP, Not Published Syngenta File N° CGA169374/1785	N	SYN
IIIA1 2.4.2/01 IIIA1 2.8.7.1/01	Krips, H.J.	1998f	Determination of the emulsion properties of A 7402 G and the pH of an aqueous dispersion of A 7402 G Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235744 GLP Not Published Syngenta File N° CGA169374/1952	N	SYN
IIIA2 2.4.2/01	Kundel, P.	1999a	Report on physico-chemical characterisation (pH value) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland Report No 72575 GLP, Not Published Syngenta File N° CGA169374/1774	N	SYN

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IIIA1 2.5.2/01	Krips, H.J.	1998g	Report on determination of the viscosity Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235711 GLP Not Published Syngenta File N° CGA169374/1868	N	SYN
IIIA2 2.5.2/01	Martin, N.	1999a	Final report on viscosity of liquids Novartis Crop Protection AG, Basel, Switzerland Novartis Services AG, Basel, Switzerland Report No PP-99/25C.VIL GLP, Not Published Syngenta File N° CGA169374/1772	N	SYN
IIIA1 2.5.3/01	Krips, H.J.	1998h	Report on determination of the surface tension of an aqueous solution Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235722 GLP Not Published Syngenta File N° CGA169374/1869	N	SYN
IIIA2 2.5.3/01	Martin, N.	1999b	Final report on surface tension Novartis Crop Protection AG, Basel, Switzerland Novartis Services AG, Basel, Switzerland Report No PP-99/26C.SUR GLP, Not Published Syngenta File N° CGA169374/1773	N	SYN
IIIA1 2.7.1/01	Krips, H.J.	1998i	Determination of the accelerated storage stability of A7402G Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235812 GLP Not Published Syngenta File N° CGA169374/1865	N	SYN
IIIA1 2.7.1/02	Kundel, P.	1999a	Report on product stability (18 weeks 30°C, fluorinated high density polyethylene pack) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Müncwilen AG, Müncwilen, Switzerland, Report No 18220283 GLP Not Published Syngenta File N° CGA169374/1875	N	SYN
IIIA2 2.7.1/03	Kundel, P.	1999b	Report on product stability Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Müncwilen AG, Müncwilen, Switzerland, Report No 18215609 GLP Not Published Syngenta File N° CGA169374/1873	N	SYN

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IIIA2 2.7.1/01	Kundel, P.	1999b	Report on chemical stability after storage (2 weeks 54°C) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No 72585 GLP, Not Published Syngenta File N° CGA169374/1812	N	SYN
IIIA2 2.7.1/02	Kundel, P.	1999c	Report on product stability (18 weeks 30°C, high density polyethylene pack) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No 19314753 Not GLP, Not Published Syngenta File N° CGA169374/1936	N	SYN
IIIA2 2.7.1/03	Kundel, P.	1999d	Report on product stability (18 weeks 30°C, steel drum with inner varnish) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No 19314776 Not GLP, Not Published Syngenta File N° CGA169374/1935	N	SYN
IIIA1 2.7.2/01 IIIA1 2.8.2/01	Krips, H.J.	1998j	Determination of the low temperature stability and persistent foaming of A7402G Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235733 GLP Not Published Syngenta File N° CGA169374/1867	N	SYN
IIIA2 2.7.2/01 IIIA2 2.8.3/01 IIIA2 2.8.5/02	Kalt, R.	1999b	Final report on physico-chemical properties (suspensibility, spontaneity of dispersion, low temp. stability, wet sieve test) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No 72577 Not GLP, Not Published Syngenta File N° CGA169374/1803	N	SYN
IIIA1 2.7.3/01	Kundel, P.	2000a	Report on product stability of A7402G after 2 Years storage at 20°C Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland, Report No 37094995 GLP Not Published Syngenta File N° CGA169374/2083	N	SYN

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IIIA1 2.7.3/02	Kundel, P.	2000b	Report on product stability of A7402G after 2 years storage at 20°C Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland, Report No 30140309 GLP Not Published Syngenta File N° CGA169374/2084	N	SYN
IIIA2 2.7.3/01	Kundel, P.	2001a	Report on product stability (2 years 20°C, high density polyethylene pack) Syngenta Crop Protection AG, Basel, Switzerland Syngenta Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No 48753463 Not GLP, Not Published Syngenta File N° CGA169374/2148	N	SYN
IIIA2 2.7.3/02	Kundel, P.	2001b	Report on product stability (2 years 20°C, steel drum with inner varnish) Syngenta Crop Protection AG, Basel, Switzerland Syngenta Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No 48779631 Not GLP, Not Published Syngenta File N° CGA169374/2149	N	SYN
IIIA1 2.1/01 IIIA1 2.6.1/01	Krips, H.J.	1998b	Determination of appearance and density of A 7402 G Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235676 GLP Not Published Syngenta File N° CGA169374/1951	N	SYN
IIIA2 2.1/01 IIIA2 2.8.2/01 IIIA2 2.8.5/01 IIIA2 2.8.8.2/01	Kalt, R.	1999a	Report on technical characteristics (appearance, odour, wet sieve test, persistent foam, pourability) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No 72576 GLP, Not Published Syngenta File N° CGA169374/1743	N	SYN
IIIA1 2/01	Krips, H.J.	1998a	Determination of the content of CGA 169374 in A 7402 G Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235665 GLP Not Published Syngenta File N° CGA169374/1950	N	SYN

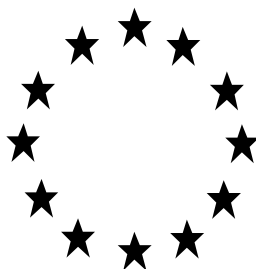
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IIIA2 2/01 IIIA2 2.6.1/01	Käser, W.	1999	Report on chemical composition (Batch : P.902001) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland Report No 72664 GLP, Not Published Syngenta File N° CGA169374/1758	N	SYN
IIIA1 2/02	Käser, W.	1999	Report on chemical composition A-7402 G (batch: P.706093) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland, Report No 72974 GLP Not Published Syngenta File N° CGA169374/1961	N	SYN
IIIA1 2/03	Stampf, Ph.	2002	Chemical composition A-7402 G Syngenta Crop Protection AG, Basel, Switzerland Syngenta Crop Protection Münchwilen AG, Münchwilen, Switzerland, Report No 108331 GLP Not Published Syngenta File N° CGA169374/2244	N	SYN
IIIA2 2.10/01	Kalt, R.	1999c	Report on physico-chemical properties (distribution on seed) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland Report No 72579 GLP, Not Published Syngenta File N° CGA169374/1718	N	SYN

* Protection for 5 years claimed from date of decision concerning listing in Annex I - the study report has not been submitted any of the Member States in support of an application for authorization, or (though the study report has been submitted) has not been used any of the Member States as the basis for decision on the initial authorization, or to maintain a given authorization, of a plant protection product before the date of submission of the dossier to Rapporteur Member State.

† Owners' code identifications and names (Code identification: SYN, Name: Syngenta Limited)

Draft Assessment Report



DIFENOCONAZOLE

Volume 3

Annex B.3

Data on application and further information

Rapporteur Member State: Sweden

May 2006

Updated December 2006

Volume 1

Level 1: Statement of subject matter and purpose for which the monograph was prepared

Level 2: Reasoned statement of the overall conclusions drawn by the Rapporteur Member State

Appendix 1: Standard terms and abbreviations

Appendix 2: Specific terms and abbreviations

Appendix 3: List of endpoints

Level 3: Proposed decision with respect to the application for inclusion of the active substance in Annex I

Level 4: Further information to permit a decision to be made, or to support a review of the conditions and restrictions associated with the proposed inclusion in Annex 1

Volume 2

Annex A: List of the tests and studies submitted and of information available

Volume 3

Annex B: RMS summary, evaluation and assessment of the data and information

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Annex B.2: Phys/chem.

Annex B.3: Data application and further information.

Annex B.4: Proposal for classification and labelling

Annex B.5: Analytical method

Annex B.6: Toxicology and metabolism

Annex B.7: Residues in crop

Annex B.8: Fate and behaviour

Annex B.9: Ecotoxicology

Appendix 1: Standard terms and abbreviations

Appendix 2: Specific terms and abbreviations

Volume 4

Annex C: Confidential information and summary and assessment of information relating to the collective submission of dossiers

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Annex B.3: Data on application and further information

B.3 Data on application and further information**B.3.1 Data on application relevant to the active substance (Annex IIA 3.1 to 3.6)****B.3.1.1 Function**

Fungicide.

B.3.1.2 Effects on harmful organisms

Difenoconazole is a broadspectrum systemic fungicide and belongs to the group of triazole fungicides. It is active against important fungi from the classes of Ascomycetes, Basidiomycetes and Deuteromycetes.

B.3.1.2.1 Nature of the effects on harmful organisms

Difenoconazole acts by interference with the ergosterol biosynthesis in target fungi by inhibition of the C-14-demethylation of sterols, which leads to morphological and functional changes of the fungal cell membrane.

B.3.1.2.2 Translocation in plants

Systemic.

B.3.1.3 Field of use envisaged

Agriculture.

B.3.1.4 Harmful organisms controlled and crops or products protected or treated

Difenoconazole controls a broad-spectrum of foliar, seed and soil-borne diseases, caused by Ascomycetes, Basidiomycetes and Deuteromycetes, in cereals, soya, rice, grapes, pome fruit, stone fruit, potatoes, sugar beet and several vegetable and ornamental crops. It is applied by foliar spray or seed treatment.

B.3.1.4.1 Intended crop uses

The representative uses for the re-registration of difenoconazole are carrots and pomefruits for foliar uses and cereals for seed treatment use, respectively.

B.3.1.4.2 Harmful organisms controlled

Difenoconazole is a fungicide against fungal pests including *Alternaria spp.*, *Cercospora beticola*, *Colletotrichum lindemuthianum*, *Cyloconium oleaginum*, *Erysiphe spp.*, *Gugnardia bidwelli*, *Leptosphaeria*

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maculans, *Monilia laxa*, *Mycosphaerella* spp., *Phoma* spp., *Podosphaera leucotricha*, *Pseudopeziza tracheiphila*, *Puccinia* spp., *Ramularia biticola*, *Septoria* spp., *Sphaerotheca pannosa*, *Stemphylium* spp., *Uncinula necator* and *Venturia* spp.

B.3.1.4.3 Effects achieved

Morphological and functional changes of the fungal cell membrane.

B.3.1.5 Mode of action

Difenoconazole has systemic properties. Although it has protective and curative activity, it is recommended to apply products containing difenoconazole early to avoid the build-up of the disease.

B.3.1.5.1 Biochemical and physiological mechanism(s) and biochemical pathway(s) involved

Difenoconazole acts on the fungal pathogen during penetration and haustoria formation. Difenoconazole acts on target fungi by interference with the ergosterol biosynthesis by inhibition of the C-14-demethylation of sterols, which leads to morphological and functional changes of the fungal cell membrane.

B.3.1.5.2 Metabolism to the active substance

The effects of difenoconazole are not achieved as a result of the formation of active metabolites or degradation products.

B.3.1.5.3 Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies

Difenoconazole belongs to the class of triazole fungicides, which represents one of the most potent classes of fungicides available to the grower for the control of many economically important pathogens. It is in the best interest of all those involved in recommending and using these fungicides that they are utilised in such a way that their effectiveness is maintained.

Recommendations for appropriate management strategies have been made available by the FRAC-SBI Working Group and upon the work of non-industry collaborators. The recommendations are publicly available on the internet under the following address: http://www.frac.info/sbi_wg.html.

DIFENOCONAZOLE

Annex B.3: Data on application and further information

B.3.2 Data on application relevant to the plant protection products (Annex IIIA 3)**B.3.2.1 Field of use envisaged**

Agriculture.

B.3.2.2 Effects on harmful organisms

The active ingredient in A-9142 G (DIVIDEND® 030FS) and A-7402 T (SCORE® 250 EC), difenoconazole, is a broadspectrum systemic fungicide and belongs to the group of triazole fungicides. It is active against important fungi from the classes of Ascomycetes, Basidiomycetes and Deuteromycetes. It acts by interference with the ergosterol biosynthesis in target fungi by inhibition of the C-14-demethylation of sterols, which leads to morphological and functional changes of the fungal cell membrane.

B.3.2.3 Details of intended use**DIVIDEND 030FS**

Crop	Crop code	Disease	Disease code
Barley	HORSS	<i>Pyrenophora graminea</i>	PYREGR
Rye	SECCE	<i>Fusarium spp.</i> <i>Urocystis occulata</i>	FUSASP UROCAG
Triticale	TTLSS	<i>Fusarium spp.</i> <i>Tilletia caries</i>	FUSASP TILLCA
Wheat	TRZSS	<i>Fusarium spp.</i> <i>Tilletia caries</i>	FUSASP TILLCA
Oat	AVESS	<i>Ustilago avenae</i> <i>Pyrenophora avenae</i> <i>Cochliobolus sativum</i> <i>Fusarium culmorum</i> <i>Gibberella avenacea</i> <i>Pythium ultimum</i>	USTIAV PYRNAV COCHSA FUSACU GIBBAV PYTHUL

SCORE 250EC

Crop	Crop code	Disease	Disease code
Apple	MABSS	<i>Podosphaera leucotricha</i> <i>Venturia inaequalis</i>	PODOLE VENTIN
Asparagus	ASPOF	<i>Puccinia asparagi</i> <i>Stemphylium spp.</i>	PUCCAS STEMSP
Banana	MUBSS	<i>Mycosphaerella fijensis</i>	MYCOFI
Bean	PHSSS	<i>Colletotrichum lindemuthianum</i>	COLLLD
Brassicas, leafy	BRSCH	<i>Alternaria spp.</i>	ALTESP
Broccoli	BRSOK	<i>Alternaria spp.</i>	ALTESP
Brussels sprouts	BRSOB	<i>Alternaria brassicae</i> <i>Mycosphaerella brassicicola</i>	ALTEBA MYCOBR
Cabbage, head	BRSOL	<i>Alternaria brassicae</i> <i>Mycosphaerella brassicicola</i>	ALTEBA MYCOBR
Carrot	DAUSS	<i>Alternaria dauci</i> <i>Erysiphe heraclei</i>	ALTEDA ERYSHE
Cauliflower	BRSOB	<i>Alternaria spp.</i> <i>Mycosphaerella brassicicola</i>	ALTESP MYCOBR
Celery	APUSS	<i>Septoria spp.</i>	SEPTSP
Chicory witloof	CICIF	<i>Alternaria cichorii</i> <i>Erysiphe cichoracearum</i>	ALTECC ERYSCI

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Annex B.3: Data on application and further information

Crop	Crop code	Disease	Disease code
Grapes	VITVI	<i>Puccinia hieracii</i>	PUCCHI
		<i>Gugnardia bidwelli</i>	GUIGBI
		<i>Pseudopeziza tracheiphilia</i>	PSPZTR
		<i>Uncinula necator</i>	UNCINE
Lettuce	LACSA	<i>Alternaria spp.</i>	ALTESP
Olives	OLVSS	<i>Cycloconium oleaginum</i>	CYCLOL
Ornamentals	Various	<i>Erysiphe polyphaga</i>	ERYSP
		<i>Puccinia spp.</i>	PUCOSP
Pea	PIPSS	<i>Erysiphe polygoni</i>	ERYSP
Pear	PYUSS	<i>Venturia spp.</i>	VENTPI
Potato	SOLTU	<i>Alternaria solani</i>	ALTESO
Rape, oilseed	BRSNN	<i>Alternaria spp.</i>	ALTESP
		<i>Leptosphaeria maculans</i>	LEPTMA
Stonefruit	NNNOS	<i>Monilia laxa</i>	MONILA
		<i>Sphaerotheca pannosa</i>	SPHRPA
Sugarbeet	BEAVA	<i>Cercospora beticola</i>	CERCBE
		<i>Erysiphe betae</i>	ERYSBE
		<i>Ramularia biticola</i>	RAMUBE
Sunflower	HELAN	<i>Phoma spp</i>	PHOMSP
Tomato	LYPES	<i>Alternaria solani</i>	ALTESO

B.3.2.4 Application rate

DIVIDEND 030FS

The application rate of A-9142 G is 0.2 L product/100 kg seeds, equivalent to 6 g difenoconazole/100 kg seeds.

SCORE 250EC

A-7402 T will be applied at rates of maximum 0.5 L product/ha in carrots, equivalent to 125 g difenoconazole/ha. In pomefruit the maximum rate in Southern Europe is 0.3 L product/ha, equivalent to 75 g difenoconazole/ha, and 0.225 L product/ha in Northern Europe, equivalent to 56.25 g difenoconazole/ha.

Crop	Country	Formulation	Application				
			Method	Rate per application	Water volume in L/ha	Number (maximum)	PHI (days)
Carrot	EU (N, S)	A-7402 T	Foliar	125 g ai/ha	100 - 500	3	14
Pomefruit	EU (N)	A-7402 T	Foliar	56.25 g ai/ha	500-1500	4	28
Pomefruit	EU (S)	A-7402 T	Foliar	75 g ai/ha	500-1000	4	14

N=North, S=South

B.3.2.5 Concentration of active substance in material used (e.g., in the diluted spray, baits or treated seed)

DIVIDEND 030FS

A-9142 G is normally applied undiluted to the seeds.

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SCORE 250EC

The concentration of the active substance difenoconazole in the spray solution ranges between 3.75 g/hL and 7.5 g/hL in pomefruit and 25 – 125 g/hL for the use in carrot, respectively.

B.3.2.6 Method of application**DIVIDEND 030FS**

A-9142 G is applied as seed-treatment through a range of continuous flow or batch-type commercially available seed treatment machinery.

SCORE 250EC

A-7402 T is applied via tractor / vehicle mounted airblast or boom sprayers (with or without air assistance), using water volumes between 500 and 1500 L/ha. It can also be applied with hand held application devices.

B.3.2.7 Number and timing of applications**DIVIDEND 030FS**

A-9142 G is applied once as a seed treatment to cereal seeds.

SCORE 250EC

A-7402 T will be applied on carrots up to 3 times and on pomefruit up to 4 times at intervals of 10-14 days.

B.3.2.8 Growth stages of the crop or plants to be protected - For each application**DIVIDEND 030FS**

Seed treatment.

SCORE 250EC

The growth stage at application is BBCH 61. Best results are obtained when the product is applied at the onset of disease development.

B.3.2.9 Duration of protection afforded by each application**DIVIDEND 030FS**

A-9142 G is intended for protection of the crop against diseases in the early establishment phase.

SCORE 250EC

No information submitted.

DIFENOCONAZOLE

Annex B.3: Data on application and further information

B.3.2.10 Necessary waiting periods or other precautions to avoid phytotoxic effects on succeeding crops**DIVIDEND 030FS**

No waiting periods are necessary after the use of A-9142 G.

SCORE 250EC

There are no waiting periods or other particular restrictions following the use of A-7402 T in pomelo and carrots.

B.3.2.11 Proposed instructions for use

Instructions for use (copies of existing or proposed labels) were enclosed in the Dossier Documents C.

B.3.3 Summary of data on application

Products with difenoconazole are to be used for seed treatment in cereals, and for foliar applications in orchards and agricultural field crops.

The representative formulations Dividend 030FS and Score 250EC contains difenoconazole, a fungicide that is effective against a broad range of fungal pests.

The total maximum application rate of difenoconazole is 60 mg as/kg seed for seed treatment and max 3 applications of 125 g as/ha for foliar application.

Dividend 030FS is applied undiluted to cereal seeds, while Score 250EC are applied as spray solution ranging between 3.75 g/hL and 7.5 g/hL in pomelo and 25 – 125 g/hL for the use in carrot, respectively.

According to the notifier, use of products with difenoconazole according to the proposed GAP does not represent a hazard to rotational crops and does not justify a specific labelling.

B.3.4 Further information on the active substance (Annex IIA 3.7 to 3.9)**B.3.4.1 Recommended methods and precautions concerning handling, storage, transport or fire****Handling and storage :**

Avoid contact with skin, eyes and clothing. Avoid inhalation by dust. Do not eat, drink or smoke while working.

Store the product in closed original containers. Protect from light and humidity. Store separately from feed, food and stimulants.

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Annex B.3: Data on application and further information

Transport information:	Use unbreakable containers, make sure they cannot fall, and label in accordance with regulations.
Fire:	<p>Extinguishing media:</p> <p>Dry chemical extinguisher, foam, carbon dioxide or water spray (do not use direct jet of water)</p> <p>Combustion gases:</p> <p>Difenoconazole contains the elements carbon, hydrogen, chlorine, nitrogen and oxygen. In the event of fire the formation of carbon monoxide, carbon dioxide, hydrogen cyanide, hydrochloric acid and nitrogen oxides must be anticipated.</p> <p>The combustion products are toxic and/or irritant.</p>

B.3.4.2 Procedures for destruction or decontamination**B.3.4.2.1 Controlled incineration**

The active substance, difenoconazole, can be disposed of safely by incineration in a modern incinerator, licensed to treat special contaminated waste, which fulfils the following conditions: > 800°C, minimum residence time within the incinerator, 2 seconds, equipped with a washing unit for flue gases. The ashes have to be disposed of at a suitable, approved waste disposal site. Wash water has to be disposed of via a suitable waste water treatment plant.

A temporary formation of polyhalogenated dibenzo-p-dioxins and dibenzo-furans during incineration cannot be completely excluded, although the halogen content of difenoconazole is only 17.5% and therefore well below the critical limit of 60%. However, temporarily formed polyhalogenated dibenzo-p-dioxins and dibenzo-furans are destroyed completely at temperature above 800°C.

B.3.4.2.1.1 Package product wastes:

No other methods are proposed to dispose of the active substance difenoconazole. Where larger quantities are concerned, consult the supplier.

B.3.4.3 Emergency measures in the case of an accident**Clean up methods:**

Cover spillages with moist sand, earth or sawdust. Transfer to a container for disposal. Wash the spillage area with water. Washings must be prevented from entering surface water drains.

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Annex B.3: Data on application and further information

Procedures for the decontamination of water in the case of an accident:

Contaminated water must be contained. It may be decontaminated by filtration using charcoal and then concentrated. The water should be incinerated. The charcoal can be disposed of in a suitable waste incineration plant in accordance with official regulations.

B.3.5 Further information on the plant protection product (Annex IIIA 4)**B.3.5.1 Packaging (type, material, size, etc.), compatibility of the preparation with proposed packaging materials****B.3.5.1.1 Description of the packaging**

DIVIDEND 030FS

Primary container (Kolberg 1999a)

Type:	Canister
Material:	High density polyethylene
Dimensions:	190 x 140 x 280 mm
Filling quantity:	5 litre
Closure:	Screw cap, 63 mm Ø with tamper evident ring

Primary container (Kolberg 1999b)

Type:	Canister with 2 orifices
Material:	High density polyethylene
Dimensions:	275 x 232 x 394 mm
Filling quantity:	20 litre
Closure:	Screw cap closure with tamper evident ring

SCORE 250EC

Primary container

Type:	Bottle
Material:	Co-extruded high density polyethylene/polyamide (PE/PA)
Dimensions:	200 x 70 x 100 mm
Filling quantity:	1 litre
Closure:	Screw cap closure (50 mm Ø) with tamper evident ring

Primary container

Type:	Canister
Material:	Fluorinated polyethylene or co-extruded polyethylene/polyamide (PE/PA)

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Dimensions: 190 x 140 x 280 mm
Filling quantity: 5 litre
Closure: Screw cap closure (63 mm Ø) with induction heat seal and tamper evident ring

Primary container (Kolberg 1999c)

Type: Steel drum with bungs
Material: Steel with inner varnish
Dimensions: 600 mm Ø and 880 mm height
Filling quantity: 200 litre
Closure: 2 bungs of 2 and ¾ inch Ø

B.3.5.1.2 Suitability of the packaging**DIVIDEND 030FS**

The suitability of the packagings has been successfully tested according to following ADR methods:
for the 5 L and the 20 l HDPE canister: 3552 and 3555 for the 200 L steel drum: -3552, 3553, 3554 and 3555
(Kolberg 1999a, b, c)

After storage for 2 years at 20°C the packaging material:

- HDPE (high density polyethylene)
- Steel drum with inner varnish

proved to be resistant to its content.

The studies have been carried out according to GIFAP Monograph 17, and were conducted in accordance to GLP (Degen 2001a, b).

SCORE 250EC

The suitability of the packaging has been successfully tested according to the ADR methods 3552 and 3555. Other ADR methods e.g. 3553, 3554, 3556, 3558 and 3560 do not apply for this type of packaging and formulation (Krips 2000a, b).

After storage for 2 years at 20°C the packaging materials; fluorinated high density polyethylene and high density polyethylene pack, with additional barrier material (polyamide), proved to be resistant to its content A-7402-G. (Tested according to GIFAP Monograph 17). Due to its almost identical composition this will also be valid for A-7402 T (Rodler 2000a, b).

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Annex B.3: Data on application and further information

B.3.5.2 Procedures for cleaning application equipment**DIVIDEND 030FS**

Immediately after use, clean spray equipment thoroughly. Rinse the apparatus with excess water until it is visually clean. The effectiveness of the cleaning procedure can be inspected visually. If no residue is left in the equipment, all formulation has been removed.

Contamination of operators may occur not only during use of pesticides but also during removal of protective equipment and clothing after use. All such equipment and clothing should be carefully removed wearing gloves and placed in plastic bags to await cleaning if this is not to be done immediately. Clothing should be folded neatly to avoid crumpling and possible damage and increased permeability to pesticides.

Normal work clothing must be washed separately from other clothing and should be kept in a separate place. Laundering of work and protective clothing should be in the usual manner and in accordance with the manufacturer's instructions and should take place after each use. Clean clothing should be stored away from contaminated clothing in a well-ventilated area separate from the chemical storage area. Damaged or heavily contaminated clothing should be discarded.

SCORE 250EC

Clean spray equipment thoroughly immediately after use. Drain the system completely and rinse spray tank, boom and nozzles two to three times with clean water until the foam and all traces of product have been removed. The effectiveness of the cleaning procedure has been investigated for a solid and a liquid formulation containing a solid and a liquid active substance.

When A-7402 T is added to the water in the spray tank, the active substance forms an emulsion. This is analogous to the situation of A-6097 G, a propiconazole 250 EC formulation, where also an emulsion of the active substance (propiconazole) is formed. In that study it could be shown, that more than 99% had been removed by this procedure. It is predicted that the effectiveness of the cleaning procedure for A-7402 T is similar to that for A-6097 G.

Contamination of operators may occur not only during use of pesticides but also during removal of protective equipment and clothing after use. All such equipment and clothing should be carefully removed wearing gloves and placed in plastic bags to await cleaning if this is not to be done immediately. Clothing should be folded neatly to avoid crumpling and possible damage and increased permeability to pesticides.

Normal work clothing must be washed separately from other clothing and should be kept in a separate place. Laundering of work and protective clothing should be in the usual manner and in accordance with the manufacturer's instructions and should take place after each use. Clean clothing should be stored away from contaminated clothing in a well-ventilated area separate from the chemical storage area. Damaged or heavily contaminated clothing should be discarded.

DIFENOCONAZOLE

Annex B.3: Data on application and further information

B.3.5.2.1 Effectiveness of the cleaning procedures**DIVIDEND 030FS**

Effectiveness of Washing Procedures: Formulations are designed to form emulsions, suspensions or solutions by mixing with water at all relevant temperatures. Therefore it appears to be reasonable to conclude that standard washing procedures (as recommended by the manufacturer of the clothing and supported by using a detergent) are the most effective ways to clean contaminated clothing.

Protective equipment for the face and eyes such as face shields and goggles should be cleaned by wiping with a suitable detergent and a wet cloth and left to air dry. It may be necessary to clean this equipment during use to maintain clear vision. This should be done with a wet cloth and clean water. Damaged eye protection should be discarded.

Protective gloves should be rinsed with water before they are removed from the hands. At the end of each day's use, gloves and rubber boots should be washed inside and outside with detergent and water and hung up to air dry before they are used again. Clean items should be stored in a well-ventilated area separate from the chemical storage area. Damaged gloves or boots should be discarded.

SCORE 250EC

Formulations are designed to form emulsions, suspensions or solutions by mixing with water at all relevant temperatures. Therefore it appears to be reasonable to conclude that standard washing procedures (as recommended by the manufacturer of the clothing and supported by using a detergent) are the most effective ways to clean contaminated clothing.

Protective equipment for the face and eyes such as face shields and goggles should be cleaned by wiping with a suitable detergent and a wet cloth and left to air dry. It may be necessary to clean this equipment during use to maintain clear vision. This should be done with a wet cloth and clean water. Damaged eye protection should be discarded.

Protective gloves should be rinsed with water before they are removed from the hands. At the end of each day's use, gloves and rubber boots should be washed inside and outside with detergent and water and hung up to air dry before they are used again. Clean items should be stored in a well-ventilated area separate from the chemical storage area. Damaged gloves or boots should be discarded.

B.3.5.3 Pre-harvest intervals, re-entry and withholding periods, other use restrictions**DIVIDEND 030FS**

Pre-harvest intervals or re-entry periods are not relevant as A-9142 G is applied as a seed treatment.

There is no need for a waiting period between application of the product to seeds and planting of the treated seeds.

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Annex B.3: Data on application and further information

Due to the application as a seed treatment, there are no restrictions to the use of the product with regard to agricultural, environmental and plant health conditions.

SCORE 250EC

The pre-harvest interval for the use on carrots is 14 days and for the use in pomefruit 14 and 28 days in SEU and NEU, respectively. These pre harvest intervals are the basis for the proposed MRLs.

Due to the nature of the use in pome fruit and carrot, livestock is not expected to enter fields previously treated with A-7402 T.

No undue risk is expected to the re-entry worker in pome fruit and carrots when working in orchards or fields that previously have been treated with A-7402 T. However, as a basic rule, treated areas should not be re-entered before spray deposit on leaf surfaces has completely dried.

A waiting period between application and handling of treated product is not relevant due to the nature of the use as a foliar fungicide.

There is no requirement for any withholding period for animal feeding stuffs.

There is no requirement for a waiting period between application and planting of succeeding crops.

No restrictions exist for the use of A-7402 T under specific agricultural, plant health or environmental conditions. Label recommendations should always be followed in cases of shifts of sensitivity of pathogens.

B.3.5.3.1 Pre-harvest intervals, re-entry intervals or withholding periods to minimise residues in crops, plants, plant products, treated areas or spaces**DIVIDEND 030FS**

Pre-harvest intervals or re-entry periods are not relevant as A-9142 G is applied as a seed treatment.

There is no need for a waiting period between application of the product to seeds and planting of the treated seeds.

Due to the application as a seed treatment, there are no restrictions to the use of the product with regard to agricultural, environmental and plant health conditions.

SCORE 250EC

The pre-harvest interval for the use on carrots is 14 days and for the use in pomefruit 14 and 28 days in SEU and NEU, respectively. These pre harvest intervals are the basis for the proposed MRLs.

Due to the nature of the use in pomefruit and carrot, livestock is not expected to enter fields previously treated with A-7402 T.

No undue risk is expected to the re-entry worker in pome fruit and carrots when working in orchards or fields that previously have been treated with A-7402 T. However, as a basic rule, treated areas should not be re-entered before spray deposit on leaf surfaces has completely dried.

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Annex B.3: Data on application and further information

A waiting period between application and handling of treated product is not relevant due to the nature of the use as a foliar fungicide.

There is no requirement for any withholding period for animal feeding stuffs. There is no requirement for a waiting period between application and planting of succeeding crops. No restrictions exist for the use of A-7402 T under specific agricultural, plant health or environmental conditions. Label recommendations should always be followed in cases of shifts of sensitivity of pathogens.

B.3.5.3.2 Information on any specific agricultural, plant health or environmental conditions under which the preparation may or may not be used

None reported.

B.3.5.4 Statement of the risks arising and the recommended methods, precautions and procedures to minimise those risks relating to handling, storage, transport or fire

DIVIDEND 030FS

Handling and storage:

Avoid contact with skin, eyes and clothing. Avoid inhalation by dust. Do not eat, drink or smoke while working. Store the product in closed original containers. Protect from light and humidity. Store separately from feed, food and stimulants.

Transport information:

Use unbreakable containers, make sure they cannot fall, and label in accordance with regulations.

Fire:

Extinguishing media: Dry chemical extinguisher, foam, carbon dioxide or water spray (do not use direct jet of water)

Combustion gases: Difenoconazole contains the elements carbon, hydrogen, chlorine, nitrogen and oxygen. In the event of fire the formation of carbon monoxide, carbon dioxide, hydrogen cyanide, hydrochloric acid and nitrogen oxides must be anticipated.

The combustion products are toxic and/or irritant.

Personal protective Equipment:

In General: Change working clothes daily.

Breathing Protection: In case of heavy exposure, wear: Gas mask.

Eye Protection: Goggles

Hand Protection: Chemical-resistant gloves

Body Protection: Heavy duty cotton or synthetic fabric working clothes (e.g. overalls).

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Annex B.3: Data on application and further information

Precautionary measures after work: Wash thoroughly (shower, bathe, wash hair). Change clothing. Thoroughly clean protective gear. Thoroughly clean contaminated equipment with soap or soda solution. The recommended Personal Protective Equipment provides effective protection to minimize exposure during normal use and for cleaning up in the event of an accident.

Minimisation of waste:

In normal use of the product, waste should be minimized by measuring out only the quantity of product required for the area or quantity of crop requiring treatment.

SCORE 250EC

Handling and storage :

Avoid contact with skin, eyes and clothing. Avoid inhalation by dust. Do not eat, drink or smoke while working. Store the product in closed original containers. Protect from light and humidity. Store separately from feed, food and stimulants.

Transport information:

Use unbreakable containers, make sure they cannot fall, and label in accordance with regulations.

Fire:

Extinguishing media: Dry chemical extinguisher, foam, carbon dioxide or water spray (do not use direct jet of water)

Combustion gases: Difenoconazole contains the elements carbon, hydrogen, chlorine, nitrogen and oxygen. In the event of fire the formation of carbon monoxide, carbon dioxide, hydrogen cyanide, hydrochloric acid and nitrogen oxides must be anticipated.

The combustion products are toxic and/or irritant.

Personal Protective Equipment:

In General: Change working clothes daily.

Breathing Protection: In case of heavy exposure, wear: Gas mask with universal filter.

Eye Protection: Goggles or face-shield

Hand Protection: Chemical-resistant gloves

Body Protection: Heavy duty cotton or synthetic fabric impermeable working clothes (e.g. overalls). Heavy-duty shoes or boots.

Precautionary measures after work: Wash thoroughly (shower, bathe, wash hair). Change clothing. Thoroughly clean protective gear. Thoroughly clean contaminated equipment with soap or soda solution. The recommended Personal Protective Equipment provides effective protection to minimize exposure during normal use and for cleaning up in the event of an accident.

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Annex B.3: Data on application and further information

Minimisation of waste:

In normal use of the product, waste should be minimized by measuring out only the quantity of product required for the area or quantity of crop requiring treatment.

B.3.5.5 Procedures to be followed in the event of an accident during transport, storage or use**DIVIDEND 030FS****Clean up methods:**

Cover spillages with moist sand, earth or sawdust. Transfer to a container for disposal. Wash the spillage area with water. Washings must be prevented from entering surface water drains.

Procedures for the decontamination of water in the case of an accident:

Contaminated water must be contained. It may be decontaminated by filtration using charcoal and then concentrated. The water should be incinerated. The charcoal can be disposed of in a suitable waste incineration plant in accordance with official regulations.

Emergency workers should follow the recommendations for the use of Personal Protective Equipment appropriate for the handling of the undiluted product. Bystanders should be excluded from the area of an accident to prevent unnecessary exposure.

First-Aid Measures

General	Remove the affected person from the danger zone to a well-ventilated room or to fresh air, and protect from undercooling.
In case of suspected poisoning	Immediately call a physician.
Eye Contact	Rinse eyes with clean water for several minutes .
Ingestion	Repeatedly administer medicinal charcoal in a large quantity of water. NOTE; Never give anything by mouth to an unconscious person. Do not induce vomiting.
Skin Contact	Remove contaminated clothing and thoroughly wash the affected parts of the body with soap and water.
Inhalation	Immediately remove to fresh air.
Medical Instructions:	
Antidote	No specific antidote is known! Apply symptomatic therapy.
Experiences Specific to Man	No case of human poisoning is on record.

SCORE 250EC**Clean up methods:**

Cover spillages with moist sand, earth or sawdust. Transfer to a container for disposal. Wash the spillage area with water. Washings must be prevented from entering surface water drains.

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Annex B.3: Data on application and further information

Procedures for the decontamination of water in the case of an accident:

Contaminated water must be contained. It may be decontaminated by filtration using charcoal and then concentrated. The water should be incinerated. The charcoal can be disposed of in a suitable waste incineration plant in accordance with official regulations.

B.3.5.6 Procedures for destruction or decontamination of the plant protection product and its packaging**B.3.5.6.1 Neutralisation procedures for use in the event of accidental spillage**

In the event of accidental spillage of the formulated products, the neutralisation (with acid or base to neutral pH) is not an effective procedure for the destruction or decontamination of A-9142 G. Therefore, the spilled liquid formulation should first be adsorbed onto a solid, such as sand, inert clay filler, saw dust or soil, before being sweep up into a safe container to await disposal.

B.3.5.6.2 Pyrolytic behaviour of the active substance under controlled conditions at 800°C and the content of polyhalogenated dibenzo-p-dioxins in the products of pyrolysis

The halogen content of CGA 169374, which is the active substance in the formulations, is 17.5%, ie. the halogen content of the active ingredients is well below the 60 % limit. Therefore the products can be disposed of safely by incineration in an incinerator, licensed to treat contaminated waste, which fulfils the following conditions: temperature 800°C, minimum residence time within the incinerator: 2 seconds, equipped with a washing unit for flue gases. The ashes have to be disposed of at a suitable, approved waste disposal site. The wash water has to be disposed of by means of a suitable wastewater treatment plant.

B.3.5.6.3 Detailed instructions for safe disposal of the plant protection product and its packaging

The recommended method to dispose of contaminated packaging and waste is incineration. Consult the supplier where bigger quantities have to be disposed of. Contaminated steel drums must be disposed of according to local government recommended practice.

B.3.5.6.4 Methods other than controlled incineration for disposal of the plant protection product, contaminated packaging and contaminated materials

No other methods are currently available.

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Annex B.3: Data on application and further information

B.3.6 References relied on

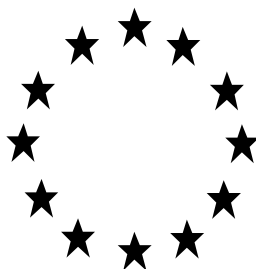
Annex No., Reference No.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	EU Data Protec- tion Claimed (Y/N)	Owner
-	Baker, S.	2004	Difenoconazole: Tier II – Document M-II, Section 1: IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, FURTHER INFORMATION AND PROPOSED CLASSIFICATION	Y	SYN
-	Baker, S.	2004	A-9142 G Difenoconazole (DIVIDEND®030 FS): Tier II – Document M-III, Section 1: IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, FURTHER INFORMATION AND PROPOSED CLASSIFICATION	N	SYN
KIIIA2 4.1.1/01 KIIIA2 4.1.2/01	Kolberg, U.	1999a	Packaging statement A-9142 G (5 lt, canister) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No N/A Syngenta File N° CGA169374/1967	N	SYN
KIIIA2 4.1.1/02 KIIIA2 4.1.2/02	Kolberg, U.	1999b	Packaging statement A-9142 G (20 lt, canister) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No N/A Syngenta File N° CGA169374/1968	N	SYN
KIIIA2 4.1.1/03 KIIIA2 4.1.2/03	Kolberg, U.	1999c	Packaging statement A-9142 G (200 lt, steel drum) Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No N/A Syngenta File N° CGA169374/1966	N	SYN
KIIIA2 4.1.3/01	Degen, S.	2001a	Report on resistance of packaging material (2 years 20°C, high density polyethylene pack) Syngenta Crop Protection AG, Basel, Switzerland Syngenta Crop Protection Mönchwil AG, Mönchwil, Switzerland Report No 72593 Not GLP, Not Published Syngenta File N° CGA169374/2150	N	SYN

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Annex B.3: Data on application and further information

KIIIA2 4.1.3/02	Degen, S.	2001b	Report on resistance of packaging material (2 years 20°C, steel drum with inner varnish) Syngenta Crop Protection AG, Basel, Switzerland Syngenta Crop Protection Münchwilen AG, Münchwilen, Switzerland Report No 72618 Not GLP, Not Published Syngenta File N° CGA169374/2151	N	SYN
-	Baker, S.	2004	A-7402 T Difenconazole (SCORE® 250 EC): Tier II – Document M-III, Section 1: IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, FURTHER INFORMATION AND PROPOSED CLASSIFICATION	N	SYN
KIIIA1 4.1.2/01	Krips, H.	2000a	Resistance of Packaging Material Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 236148 Not GLP Not Published Syngenta File N° CGA169374/2081	N	SYN
KIIIA1 4.1.2/02	Krips, H.	2000b	Resistance of packaging Material Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 236216 Not GLP Not Published Syngenta File N° CGA169374/2082	N	SYN
KIIIA1 4.1.3/01	Rodler, M.	2000a	Packaging statement A-7402 G Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland, Report No 0251 Not GLP Not published Syngenta File N° CGA169374/2086	N	SYN
KIIIA1 4.1.3/02	Rodler, M.	2000b	Packaging statement A-7402 G Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Münchwilen AG, Münchwilen, Switzerland, Report No 0280 Not GLP Not published Syngenta File N° CGA169374/2085	N	SYN

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Volume 3

Annex B.4

Proposals for classification and labelling

Rapporteur Member State: Sweden

May 2006

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Annex B.4: Proposals for classification and labelling

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WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

B.4 Proposals for classification and labelling

B.4.1 Proposals for the classification and labelling of the active substance (Annex IIA 10)

The following classification and labelling for difenoconazole was proposed by the notifier (Doc. MII: Section 1) on the basis of the available data and according to Directive 67/548/EEC.

Hazard symbol(s) :	N, Xn
Indication of danger :	Dangerous for the environment. Harmful
Risk phrases :	R 22 : Harmful if swallowed. R 50/53 : Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety phrases :	S 46 : If swallowed, seek medical advice immediately and show this container or label. S 60 : This material and its container must be disposed of as hazardous waste. S 61 : Avoid release to the environment. Refer to special instructions/Safety data sheets.

Justifications for the Proposal

Physical/chemical properties:

The active substance is not flammable. No classification required.

Health:

The toxicity of difenoconazole to mammals is summarised in annex B, section 6.10. The active substance is classified only on the basis of its acute oral toxicity (LD₅₀ 1453 mg/kg). It is not acutely toxic by the dermal or inhalation routes, is not irritating to skin or eyes, and is non-sensitising. There are also no hazard classifications based on longer-term toxicity tests.

Xn: R22 Harmful if swallowed.

Environment:

The acute toxicity of difenoconazole to aquatic organisms is summarised in Annex B, section 9.2. The active substance was classified by the notifier on the basis of its acute toxicity to fish, *Daphnia* and algae;

Species	Study type	Endpoint	Value (mg/L)	Reference
Rainbow trout	Acute static	96-h LC ₅₀	0.81	Surprenant 1987a
<i>Daphnia magna</i>	Acute	48 h LC ₅₀	0.77	Forbis 1988a
<i>Scenedesmus subscipatus</i>	Acute, static	72-h E _b C ₅₀	0.032	Grade 1993b

As all proposed endpoints were below 1.0 mg/l, the active substance was classified;

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N: R50 Very toxic to aquatic organisms

The ready biodegradability of difenoconazole is summarised in Annex B, section 8. The active substance was found to be not readily biodegradable (Baumann, 1993);

N: R53 May cause long-term adverse effects in the aquatic environment

Safety phrases

The following safety phrases are proposed on the basis of the hazards determined above;

S46 If swallowed, seek medical advice immediately and show this container or label.

S60 This material and its container must be disposed of as hazardous waste.

S61 Avoid release to the environment. Refer to special instructions/Safety data sheets.

RMS comments

Human health:

RMS agrees with the classification and labelling proposed by the notifier for the active ingredient.

Environment:

The acute data for fish referred to by the notifier was assessed as not valid by the RMS. In a more reliable study, the LC₅₀ was determined to be 1.1 mg/L (Surprenant 1990a). The values for aquatic invertebrates and algae still fulfil the criteria for R50. Hence, the RMS agrees with the classification and labelling of the active ingredient as proposed by the notifier. The modified basis for the classification is given in the table below.

Species	Study type	Endpoint	Value (mg/L)	Reference
Rainbow trout	Acute static	96-h LC ₅₀	1.1	Surprenant 1990a
<i>Daphnia magna</i>	Acute	48 h LC ₅₀	0.77	Forbis 1988a
<i>Scenedesmus subscipatus</i>	Acute, static	72-h E _b C ₅₀	0.032	Grade 1993b

B.4.2 Proposals for the classification and labelling of preparations (Annex IIA 12.3-4)

Dividend 030FS

The following classification and labelling for Dividend 030FS (A-9142 G) was proposed by the notifier (Doc. MIII, Section 1) on the basis of the available data and according to Directive 1999/45/EC:

Hazard symbol(s) :	None
Indication of danger :	Dangerous for the environment
Risk phrases :	R 52/53 : Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety phrases :	S 2 : Keep out of the reach of children
	S 13 : Keep away from food, drink and animal feeding stuffs
	S 20/21 When using do not eat, drink or smoke
	S 35 : This material and its container must be disposed of in a safe way
	S 57 : Use appropriate containment to avoid environmental contamination

Justifications for the Proposal

Physical/chemical properties:

The preparation is not flammable. No classification required.

Health:

The acute toxicity of A-9142 G to mammals is summarised in Annex B, section 6.11. It is not acutely toxic by the oral, dermal or inhalation routes, is not irritating to skin or eyes, and is non-sensitising. No additional labelling is considered required according to the safety data sheets of the formulators.

Environment:

The acute toxicity of A-9142 G to aquatic organisms is summarised in Annex B, section 9.2. The preparation is classified on the basis of its acute toxicity to fish, Daphnia and algae;

Species	Study type	Endpoint	Value (mg/L)	Reference
Rainbow trout	Acute	96-h LC ₅₀	37.5	Gries 1999a
Daphnia magna	Acute	48 h LC ₅₀	19	Gries 1999b
Scenedesmus subscipatus	Acute	72-h E _b C ₅₀	62	Gries 1999c

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As the endpoints for all species are in the range 10 - 100 mg/l, the preparation is classified;

R52 Harmful to aquatic organisms

The ready biodegradability of difenoconazole is summarised in Annex B, section 8. The active substance was found to be not readily biodegradable. As the active substance is present in the preparation at a concentration >2.5%, the preparation should be classified;

R53 May cause long-term adverse effects in the aquatic environment

Safety phrases

The following safety phrases are proposed on the basis of the hazards determined above, and for the purposes of product stewardship;

S2 Keep out of the reach of children

S13 Keep away from food, drink and animal feeding stuffs

S20/21 When using do not eat, drink or smoke

S35 This material and its container must be disposed of in a safe way

S57 Use appropriate containment to avoid environmental contamination

Risk and Safety phrases proposed in accordance with Article 16(1) of Directive 91/414/EEC

The following phrases are proposed on the basis of the hazards determined above;

SP1 Do not contaminate water with the product or its container

RMS comments

Human health:

The RMS agrees with the classification and labelling of the representative formulation Dividend 030FS as proposed by the notifier. However the safety phrases S20/21 is considered unnecessary.

Environment:

The data on toxicity to fish and aquatic invertebrates referred to by the notifier was re-evaluated by the RMS, resulting in the following values.

Species	Study type	Endpoint	Value (mg/L)	Reference
Rainbow trout	Acute	96-h LC ₅₀	23.3	Gries 1999a
Daphnia magna	Acute	48 h LC ₅₀	14	Gries 1999b
Scenedesmus subscipatus	Acute	72-h E _b C ₅₀	62	Gries 1999c

The modified values still fulfil the criteria for R52, and hence the RMS agrees with the classification and labelling of the representative formulation Dividend 030FS as proposed by the notifier.

Classification and labelling for Dividend 030FS as proposed by the RMS:

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Hazard symbol(s) :	None
Indication of danger :	Dangerous for the environment
Risk phrases :	R 52/53 : Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety phrases :	S 2: Keep out of the reach of children
	S13: Keep away from food, drink and animal feeding stuffs
	S 35 : This material and its container must be disposed of in a safe way
	S 57 : Use appropriate containment to avoid environmental contamination

Score 250EC

The following classification and labelling for Score 250EC (A-7402 T) was proposed by the notifier (Doc. MIII, Section 1) on the basis of the available data and according to Directive 1999/45/EC:

Hazard symbol(s) :	N
Indication of danger :	Dangerous for the environment
Risk phrases :	R 50/53 : Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety phrases :	S 2 : Keep out of the reach of children
	S 13 : Keep away from food, drink and animal feeding stuffs
	S 20/21 When using do not eat, drink or smoke
	S 35 : This material and its container must be disposed of in a safe way
	S 57 : Use appropriate containment to avoid environmental contamination

Justifications for the Proposal**Physical/chemical properties:**

The preparation is not flammable. No classification required.

Health:

The acute toxicity of A-7402 T to mammals is summarised in annex B, section 6.11. It is not acutely toxic by the oral, dermal or inhalation routes, is not irritating to skin or eyes, and is non-sensitising. The content of solvent (classified R65) in the preparation (Cn >10%) means that classification for aspiration hazard should be considered. Viscosity (dynamic) is at least 13 mPa.s at 40°C. Dividing by the density (1.059 g/ml) gives the kinematic viscosity = $12.3 \times 10^{-6} \text{ m}^2/\text{s}$. This is above the critical value of $7 \times 10^{-6} \text{ m}^2/\text{s}$ therefore R65 is not required. No additional labelling is considered required according to the safety data sheets of the formulators.

Environment:

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The acute toxicity of A-7402 T to aquatic organisms is summarised in Annex B, section 9.2. Tests were conducted on the variant formulation A-7402 H. The tested formulation contains a different but comparable solvent system to A-7402 T, therefore the results are considered relevant for the classification of A-7402 T. The preparation is classified on the basis of its acute toxicity to fish, Daphnia and algae;

Species	Study type	Endpoint	Value (mg/L)	Reference
Rainbow trout	Acute	96-h LC ₅₀	7.4	Rufli 1994
Daphnia magna	Acute	48 h LC ₅₀	3.8	Voigt 1990b
<i>Scenedesmus subscipatus</i>	Acute	72-h EbC ₅₀	0.15	Grade 1994b

As the proposed endpoint for algae was below 1.0 mg/l, the preparation was classified;

N: R50 Very toxic to aquatic organisms

The ready biodegradability of difenoconazole is summarised in Annex B, section 8. The active substance was found to be not readily biodegradable. As the active substance is present in the preparation at a concentration >2.5%, the preparation should be classified;

N: R53 May cause long-term adverse effects in the aquatic environment

Safety phrases

The following safety phrases are proposed on the basis of the hazards determined above, and for the purposes of product stewardship;

S2 Keep out of the reach of children

S13 Keep away from food, drink and animal feeding stuffs

S20/21 When using do not eat, drink or smoke

S35 This material and its container must be disposed of in a safe way

S57 Use appropriate containment to avoid environmental contamination

Risk and Safety phrases proposed in accordance with Article 16(1) of Directive 91/414/EEC

The following phrases are proposed on the basis of the hazards determined above;

SP1 Do not contaminate water with the product or its container

RMS comments

Human health:

The RMS agrees with the classification and labelling of the representative formulation Score 250 EC as proposed by the notifier. However the safety phrases S20/21 is considered unnecessary.

Environment:

The data referred to in the notifier's proposal was based on studies on a formulation assessed as not comparable to the representative formulation. Data from valid studies are given below.

Species	Study type	Endpoint	Value (mg/L)	Reference
Rainbow trout	Acute	96-h LC ₅₀	2.6	Voigt 1990a
Daphnia magna	Acute	48 h LC ₅₀	4.3	Volz 2004

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<i>Scenedesmus subscipatus</i>	Acute	72-h EbC50	6.4	Peters 1992
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As all the relevant data were between 1 – 10 mg/L, this formulation fulfils the criteria for R51, and not R50 as proposed by the notifier. **The RMS proposal for classification is as follows:**

Hazard symbol(s) : N

Indication of danger : Dangerous for the environment

Risk phrases : **R 51/53 :** Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Safety phrases : **S 2:** Keep out of the reach of children

S 13: Keep away from food, drink and animal feeding stuffs

S 35 : This material and its container must be disposed of in a safe way

S 57 : Use appropriate containment to avoid environmental contamination

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DIFENOCONAZOLE
Annex B.4: Proposals for classification and labelling

B.4.3 References relied on

Annex No., Reference No.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	EU Data Protection Claimed (Y/N)	Owner
Annex II - difenoconazole					
-	Baker, S.	2004	Difenoconazole: Tier II – Document M-II, Section 1: IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, FURTHER INFORMATION AND PROPOSED CLASSIFICATION	N	SYN
KIIA 5.2.1/01	Argus, MA, Ricci, JM, Huber, KR, Schiavo, DM, Hazelette, JR, Green, JD	1987	CGA 169374 tech.: Acute oral toxicity study in rats Novartis Crop Protection AG, Basel, Switzerland [REDACTED] Report No MIN 862119 GLP Not Published Syngenta File N° CGA169374/0247	N	SYN
KIIA 8.2.4/01	Forbis, A.D.	1988a	Acute toxicity of CGA 169374 to Daphnia magna Novartis Crop Protection AG, Basel, Switzerland ABC Analytical Bio-Chemistry Lab. Inc., Columbia United States, Report No 34835 GLP Not Published Syngenta File N° CGA169374/0021	N	SYN
KIIA 8.2.6/02	Grade, R.	1993b	Report on the growth inhibition test of CGA 169374 tech. to green algae (Scenedesmus subspicatus) Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Basel, Oekotoxikologie, Basel, Switzerland, Report No 938153 GLP Not Published Syngenta File N° CGA169374/0860	N	SYN
Annex III – DIVIDEND 030FS					
-	Baker, S.	2004	A-9142 G Difenoconazole (DIVIDEND®030 FS): Tier II – Document M-III, Section 1: IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, FURTHER INFORMATION AND PROPOSED CLASSIFICATION	N	SYN
KIIIA2 10.2.1/01	Gries, Th.	1999a	Acute Toxicity test of CGA 169374 FS 30 (A9142 G) to Rainbow trout (Oncorhynchus mykiss) under static conditions Novartis Crop Protection AG, Basel, Switzerland [REDACTED] Report No 1047.062.103 GLP Not Published Syngenta File N° CGA169374/1907	N	SYN

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DIFENOCONAZOLE

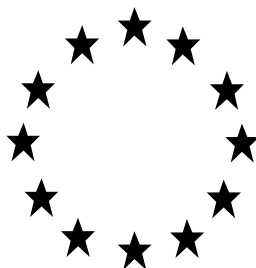
Annex B.4: Proposals for classification and labelling

KIIIA2 10.2.1/02	Gries, Th.	1999b	Acute Toxicity test of CGA 169374 FS 30 (A9142 G) to daphnids (<i>Daphnia magna</i>) under static conditions Novartis Crop Protection AG, Basel, Switzerland Springborn Smithers Laboratories (Europe) AG, Horn, Switzerland, Report No 1047.062.110 GLP Not Published Syngenta File N° CGA169374/1908	N	SYN
KIIIA2 10.2.1/03	Gries, Th.	1999c	Toxicity test of CGA 169374 FS 30 (A9142 G) to the freshwater algae <i>Pseudokirchneriella subcapitata</i> Novartis Crop Protection AG, Basel, Switzerland Springborn Smithers Laboratories (Europe) AG, Horn, Switzerland, Report No 1047.062.430 GLP Not Published Syngenta File N° CGA169374/1906	N	SYN
Annex III – SCORE 250EC					
-	Baker, S.	2004	A-7402 T Difenconazole (SCORE®250 EC): Tier II – Document M-III, Section 1: IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, FURTHER INFORMATION AND PROPOSED CLASSIFICATION	N	SYN
KIIIA1 10.2.1/01	Voigt, H.	1990a	Toxizität von CGD 96 430 F für Regenbogenforellen <i>Salmo gairdnerii</i> (4 Tage) Novartis Crop Protection AG, Basel, Switzerland [REDACTED] Report No 05/90/232 GLP Not Published Syngenta File N° CGA169374/0761	N	SYN
KIIIA 10.2.1/02	Volz, E	2004	Difenconazole 250 EC formulation (A7402T): Acute toxicity to <i>Daphnia magna</i> in a 48 hour immobilization test. RCC Ltd. Switzerland Report No. 853039 Not published GLP Syngenta File No. CGA169374/2552	N	SYN
KIIIA1 10.2.1/07	Peters, A.	1992	CGA 169374 Toxizität von CGD 96430 F auf <i>Scenedesmus subspicatus</i> CHODAT (96 h) Novartis Crop Protection AG, Basel, Switzerland Oekolimna, Burgwedel, Germany, Report No N/A GLP Not Published Syngenta File N° CGA169374/0630	N	SYN

*: Protection for 5 years claimed from date of decision concerning listing in Annex I - the study report has not been submitted any of the Member States in support of an application for authorization, or (though the study report has been submitted) has not been used any of the Member States as the basis for decision on the initial authorization, or to maintain a given authorization, of a plant protection product before the date of submission of the dossier to Rapporteur Member State.

** : Owners' code identifications and names (Code identification: AKA, STI
Name: Agro Kanesho, Stähler International GmbH & Co. KG)

Draft Assessment Report



DIFENOCONAZOLE

Volume 3 Annex B.5 Analytical methods

Rapporteur Member State: Sweden

May 2006

Volume 1

Level 1: Statement of subject matter and purpose for which the monograph was prepared

Level 2: Reasoned statement of the overall conclusions drawn by the Rapporteur Member State

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Annex B.3: Data application and further information.

Annex B.4: Proposal for classification and labelling

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Annex C: Confidential information and summary and assessment of information relating to the collective submission of dossiers

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B.5 Methods of Analysis

B.5.1 Analytical methods for formulation analysis (Annex IIA, 4.1, Annex IIIA, 5.1)

B.5.1.1 Analytical methods for the determination of the active substance in the active substance as manufactured

Reference: 1. **Kaesler, W., (2000a)** Analytical Method CGA 169374 tech. Novartis Crop Protection Munchwilen AG, Munchwilen, Switzerland, unpublished, Method No. AW-128/3, Issued 28/08/2000 Syngenta File No. CGA 169374/2064.

2. **Käser, W., (2000b)** Validation of Analytical Method AW-128/3 Novartis Crop Protection Munchwilen AG, Munchwilen, Switzerland Not GLP, unpublished, Report No. 81931, Issued 22/08/2000 Syngenta File No. CGA 169374/2440

Method: The active substance difenoconazole is determined in technical material (dissolved in acetone) by gas chromatography using a wide bore DB-5 column and flame ionization detection. Quantification is by comparison of peak areas ratios to those of a reference solution.

GLP: 1. No; 2. Yes

Validation Data:

Specificity: The method has been shown to be specific for the determination of difenoconazole.

Linearity: The method has been shown to be linear over the range 0.5 to 1.50 times the recommended sample weight. The correlation coefficient (r) was 1.00000.

Accuracy: The accuracy of the method is established based on the findings for specificity, recovery and linearity. The recovery was determined using three samples spiked with 75%, 100% and 125% of the nominal amount of active substance. The mean recovery was 99.9%.

Precision (Repeatability): The repeatability was determined with five individual sub-samples of technical material. The relative standard deviation was 0.18 %.

RMS comments: Analytical method AW-128/3 is suitable for the specific and accurate determination of difenoconazole in technical material, with acceptable precision. Validation/data complies with the criteria in SANCO/3030/99 rev.4, 11/07/00.

B.5.1.2 Analytical methods for the determination of the impurities in the active substance as manufactured

Confidential information, see Annex C.

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B.5.1.3 Analytical methods for the determination of the active substance in the plant protection productDividend**Reference:**

1. Kaeser, W., (1999) Analytical Method CGA 169374 in A-9142 G by Liquid Chromatography, Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland. Not GLP, unpublished, Method No. AF - 1385/ 1, Issued 20/04/1999 Syngenta File No. CGA 169374/1779.

2. Kaeser, W., (1999a) Report on the Validation of Analytical Method AF-1385/1, Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland Not GLP, unpublished, Report No. 72771, Issued 20/04/1999. Syngenta File No. CGA 169374/2020.

Method:

The active substance difenoconazole is determined in A-9142 G (sample dissolved in water and acetonitrile and treated by ultrasonic bath and filtration/centrifugation) by liquid chromatography using a Nucleosil C18 column, acetonitrile/water mobile phase buffered at pH7 and UV detection at 240nm. Quantification is by comparison of peak areas ratios to those of a reference solution.

There is no CIPAC method available for the determination of difenoconazole and its formulations.

No toxicologically, ecotoxicologically or environmentally relevant impurities will be formed during manufacture of A-9142 G, or from degradation during storage.

GLP:

1. No; 2. Yes

Validation Data:

Full validation of method AF-1385/1 has been conducted.

Specificity:

The specificity is confirmed, no interference was observed. The method is able to separate the active substance from the formulation blank, the internal standard and the solvent.

Linearity:

The linearity was determined using five weights of formulation blank spiked with 50%, 75%, 100%, 125% and 150% of the nominal amount of active substance. The linearity was established and the coefficient of correlation (r) was calculated to be 0.99995.

Accuracy:

The accuracy of the method is established based on the findings for specificity, recovery and linearity. The recovery was determined using three weights of formulation blank spiked with 75%, 100% and 125% of the nominal amount of active substance. The mean recovery was 99.7%.

Precision (Repeatability):

The repeatability was determined with five individual sub-samples of the same batch of formulation. The relative standard deviation was 0.93 %.

RMS comments:

Analytical method AF-1385/1 is suitable for the specific and accurate determination of difenoconazole in A-9142 G, with acceptable precision (validation/data complies with the criteria in SANCO/3030/99 rev.4, 11/07/00).

Score

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Reference:	<p>1. Käser, W., (1992) Analytical Method CGA 169374 in Formulation (A-7402 G/H/K), Ciba-Geigy Münchwilen AG, Münchwilen, Switzerland, unpublished, Method No. AF - 1044/ 1, Issued 14/05/1992, Syngenta File No. CGA 169374/1027.</p> <p>2. Kaeser, W., (1994) Report on the Validation of Analytical Method AF-1044/1 Ciba-Geigy Münchwilen AG, Münchwilen, Switzerland, unpublished, Report No. 24393, Issued 14/06/1994, Syngenta File No. CGA 169374/1028.</p> <p>3. Krips, W., (1998a) Report on the Validation of Analytical Method AF-1044/1 NOTOX B.V., 'S-Hertogenbosch, Netherlands, unpublished, Report No. 235834, Issued 06/11/1998, Syngenta File No. CGA 169374/1864.</p>
Method:	<p>The active substance difenoconazole is determined in A-7402 T (dissolved in 1,2-dichlorobenzene) by gas chromatography using a wide bore SE 54 column and flame ionization detection. Quantification is by comparison of peak areas ratios to those of a reference solution.</p> <p>Whilst Method No. AF-1044/1 was originally designed for formulation A-7402 G due to the close similarity of the formulation variants (A-7402 G and T) the method remains applicable to formulation A-7402 T.</p> <p>There is no CIPAC method available for the determination of difenoconazole and its formulations.</p> <p>No toxicologically, ecotoxicologically or environmentally relevant impurities will be formed during manufacture of A-7402 T, or from degradation during storage.</p>
GLP:	1.No; 2. No; 3. No
Validation Data:	Full validation of method AF-1044/1 has been conducted and is covered in two separate reports (Kaeser, 1994 and Krips, 1998).
Specificity:	The specificity is confirmed, no interference was observed. The method is able to separate the active substance from the formulation blank, the internal standard and the solvent.
Linearity:	The linearity was determined using five weights of formulation blank spiked with 50%, 75%, 100%, 125% and 150% of the nominal amount of active substance. The linearity was established and the coefficient of correlation (r) was calculated to be 0.99981.
Accuracy:	The recovery was determined using three weights of formulation blank spiked with 75%, 100% and 125% of the nominal amount of active substance. The mean recovery was 100.0%.
Precision (Repeatability):	The repeatability was determined with five individual sub-samples of the same batch of formulation. The relative standard deviation was 0.51 %.
RMS comments:	Analytical method AF-1004/1 is suitable for the specific and accurate determination of difenoconazole in A-7402 T, with acceptable accuracy and precision. Validation/data complies with the criteria in SANCO/3030/99 rev.4, 11/07/00.

B.5.2 Analytical methods (residue) for plants, plant products, foodstuffs of plant and animal origin, feedingstuffs (Annex IIA 4.2.1; Annex IIIA 5.2)

B.5.2.1 Analytical methods for analysis of residues in food of plant origin

Reference:	Steinhauer S. (2004a) , 'Difenoconazole: Validation of the DFG Method S 19 (Extended Revision) for the Determination of residues of Difenoconazole in Apple, Oil Seed Rape, Wheat (Grain) and Lettuce'. Dr Specht & Partner Chem. Laboratorien GmbH. Unpublished Report No. SYN-0301V Az. G03-0012, Syngenta File No. CGA169374/2428.
Method:	The DFG Method S 19 (extended revision), proposed as a monitoring method, was validated for the determination of the residues of difenoconazole in apple, lettuce, wheat (grain) and oilseed rape. The extractions of the pesticide from the crop matrices were performed using acetone and ethylacetate/cyclohexane (1 +1) for apple and lettuce (extraction module E1), same solvents but different procedural details for wheat grain (module E2) and acetone/acetonitrile (1 + 9) for oil seed rape (module E7) followed by clean-up procedures according to module GPC and module C1 (silica gel mini column). Finally, high performance liquid chromatography using tandem mass spectrometric detection was used for quantitation of difenoconazole using mass transition m/z 406 -> 251 for all matrices.
GLP:	Yes.
Validation Data:	Concerning modified method (LC-MS/MS mode)
Specificity:	Demonstrated using LC-MS/MS, which is a highly specific detection technique.
Linearity:	The calibration line was linear to the naked eye and a linear equation was presented (concentration range 0.400 – 20.0 ng/ml; n=7) with r=0.9995
Accuracy:	Determined as recovery (see table below). The results show that the overall procedural recoveries for each matrix tested using the LC-MS-MS technique were within the range 70-110%, apart from lettuce overall, which was only slightly outside this range at 112% as were lettuce 0.2 mg/kg (113%) and wheat 0.05 mg/kg (114%).
Precision (Repeatability):	Repeatability was within the requirements of EU-guidance ($RSD \leq 20\%$), see table below
LOQ:	0.02 mg/kg (apple, lettuce), 0.05 mg/kg (wheat grain, oilseed rape)
LOD:	nd.

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be based on the basis of this document.

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Results:**Table B.5.2.1-1: Recovery of Difenonazole from crops**

Matrix	Forti- fication level [mg/kg]	Recoveries				No. of analyses	Overall recovery		
		single values [%]	mean [%]	Std. dev. [%]	Rel. std. dev. [%]		mean [%]	Std. dev. [%]	Rel. std. dev. [%]
Apple	0.02	75, 108, 114, 107, 108	102	16	15	5	106	11	11
	0.2	102, 108, 114, 112, 109	109	4.6	4.2	5			
Lettuce	0.02	113, 113, 113, 116, 95	110	8.5	7.7	5	112	6.7	6.0
	0.2	109, 115, 113, 108, 120	113	4.8	4.2	5			
Wheat (grain)	0.05	118, 115, 120, 110, 108	114	5.1	4.5	5	107	11	10
	0.5	116, 100, 101, 89, 91	99	11	11	5			
Oil Seed Rape	0.05	94, 97, 108, 106, 117	104	9.2	8.8	5	106	6.6	6.2
	0.5	106, 107, 106, 112, 107	108	2.5	2.3	5			

RMS comments: The results indicate that this method is appropriate for monitoring purposes ; validation/data complies with the criteria in SANCO/825/00 rev. 7, 17/03/2004, except minor deviations regarding recoveries; see also Independent Laboratory Validation (next) and "Evaluation and assessment" (chapter B5.5).

Independent Laboratory Validation

Reference: Schulz H (2004). 'Independent Laboratory Validation of DFG Method S19 (Extended Revision) for the Determination of Residues of difenoconazole in/on plant matrices', Institut Fresenius, Unpublished report IF-04/00160619. Syngenta File No. CGA169374/2507.

Method: See above.

GLP: Yes.

Validation Data:

Specificity: The MS/MS detection technique is highly specific to the desired analytes with no interferences.

Linearity: The calibration line was linear to the naked eye and a linear equation was presented (concentration range about 0.002 – 0.5 ng/ml; n=7) with r=0.99995

Accuracy: Determined as recovery (se table below). All procedural recoveries were within the range 70-110%.

Precision (Repeatability): Determined as RSD (se table below), which were <20%.

LQO: 0.01 mg/kg (apple, oilseed rape, wheat grain and lettuce).

LOD: nd.

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Results:**Table B.5.2.1-2: Recovery of Difenconazole from crops (ILV-report)**

Matrix	Fortification level mg/kg	No. of fortified specimens	Recovery range %	R _{mean} %	SD	CV %
apple	0.01	5	81 - 93	86.6	4.6	5.3
apple	0.1	5	82 - 97	89.2	7.3	8.2
overall data	0.01 + 0.1	10	81 - 97	87.9	5.9	6.7
oil seed rape	0.01	5	82 - 108	96.5	9.7	10.0
oil seed rape	0.1	5	79 - 107	95.6	11.0	11.5
overall data	0.01 + 0.1	10	79 - 108	96.1	9.8	10.2
wheat grain	0.01	5	72 - 88	81.1	6.3	7.8
wheat grain	0.1	5	68 - 81	77.2	5.7	7.3
overall data	0.01 + 0.1	10	68 - 88	79.1	6.0	7.6
lettuce	0.01	5	71 - 89	80.9	8.3	10.3
lettuce	0.1	5	72 - 96	86.6	9.3	10.7
overall data	0.01 + 0.1	10	71 - 96	83.8	8.8	10.5

RMS comments: The independent laboratory validation of this method shows that it is suitable for use as a monitoring method. Validation/data complies with the criteria in SANCO/825/00 rev. 7, 17/03/2004.

Reference: Williams W.L., Shoffner K.P. (1987). 'CGA 169374, Analytical method for the determination of CGA 169374 in tomatoes and potatoes by gas chromatography', Ciba-Geigy Corporation, Greensboro, USA, Unpublished report AG-514. Syngenta File No. CGA169374/0052

Method: AG-514, pre-registration method. A representative crop sample is extracted by refluxing in 8:2 (v/v) methanol:conc. ammonium hydroxide. After filtering, an aliquot of the extract is partitioned with hexane. The hexane fraction is partitioned with acetonitrile and the acetonitrile fraction is cleaned up on a silica gel SepPak. The final extract is analyzed by packed column gas chromatography using nitrogen phosphorus detection (GC-NPD).

GLP: No

Validation Data:

Specificity: The peak of interest was sufficiently resolved from all other peaks in the chromatograms, with no interfering peaks in the control samples.

Linearity: Method AG-537A was linear over the range of fortified samples (0.2 – 5.0 ng); $r = 0.9977$.

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Accuracy: Mean recoveries were ranging from 70 – 110% (but sample set was too small, n<10, see table below)

Precision (Repeatability): Repeatability according to summing all data was within the requirements of EU-guidance ($RSD \leq 20\%$). Repeatability specifically for green tomato fruit was somewhat outside (20.1%). The sample set was not complete.

LOQ: 0.05 mg/kg (tomato fruit, potato tuber); incomplete sample set (n < 5)

LOD: nd

Results:

Table B.5.2.1-3: Recovery of difenoconazole from potatoes and tomatoes using AG-514

Matrix	Forti- fication Level [mg/kg]	Recoveries				N
		single values [%]	mean [%]	SD [%]	RSD [%]	
Green Tomato Fruit	0.05	84	84			1
	0.10	125	125			1
	0.50	118	118			1
	Overall		109.0	21.9	20.1	3
Ripe Tomato Fruit	0.05	86	86			1
	0.10	95	95			1
	0.50	110	110			1
	Overall		97.0	12.1	12.5	3
Potato Tubers	0.05	79	79			1
	0.10	80	80			1
	0.50	96	96			1
	Overall		85.0	9.5	11.2	3

RMS comments: Method AG-514 taken separately is not considered a fully validated method for the determination of difenoconazole residues in tomatoes and potato tubers. The sample set is incomplete according to criteria in SANCO/3029/99 rev.4, 11/07/00. However, see also “Evaluation and assessment” (chapter B5.5), the results as such are acceptable.

Reference:

1. Williams W.L. (1988). ‘CGA 169374, Anal. Method for the determination of CGA 169374 in wheat raw agricultural commodities by gas chromatography’, Ciba-Geigy Corporation, Greensboro, USA, Unpublished report AG-537. Syngenta File No. CGA169374/0053.

2. Whetzel J.E. (1990). ‘Method Ruggedness Trial for Ciba-Geigy Analytical Method No. AG-537A for the Determination of CGA-169374 in Wheat Raw Agricultural Commodities by Gas Chromatography’, Ciba-Geigy Corporation, Greensboro, USA, Unpublished report AG-575A. Syngenta File No. CGA169374/0619

Method:

AG-537, pre-registration method. A representative crop sample is extracted by refluxing in 8:2 (v/v) methanol:conc. ammonium hydroxide. After filtering, an aliquot of the extract is diluted with water and saturated sodium chloride and partitioned with hexane. The hexane fraction is partitioned with acetonitrile and the acetonitrile fraction is cleaned up on a silica gel SepPak. The sample is then cleaned up on a charcoal:magnesium

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oxide: Celite column. The extract is analyzed by packed column GC-NPD.

GLP: 1. No; Yes

Validation Data: Using also AG-537A which practically is identical to AG-537

Specificity: The peak of interest was sufficiently resolved from all other peaks in the chromatograms, with no interfering peaks in the control samples (AG-537A).

Linearity: Method AG-537A was linear over the range of fortified samples (0.2 – 5.0 ng); $r = 0.99992$

Accuracy: Recoveries were within 70 – 110%, see tables below (different parts of wheat and carrots), but the sample set is too small for carrots ($n < 10$).

Precision (Repeatability): Repeatability was within the requirements of EU-guidance ($RSD \leq 20\%$) (AG-537-A), but the sample set is too small for carrots ($n < 10$).

LOQ: 0.05 mg/kg (wheat grain/straw/forage/hay) (AG-537-A).

LOD: nd

Results:

Table B.5.2.1-4: Recoveries of Difenoconazole from wheat raw agricultural commodities using AG-537

Matrix	Forti- fication level [mg/kg]	Recoveries				N
		single values [%]	mean [%]	SD [%]	RSD [%]	
Wheat Forage	0.05	109, 109	109.0	0.0	0.0	2
	0.50	82	82.0	N/A	N/A	1
	5.0	93	93.0	N/A	N/A	1
	10.0	87	87.0	N/A	N/A	1
	Overall		96.0	12.5	13.0	5
Wheat Hay	0.05	99, 99	99.0	0.0	0.0	2
	0.50	75	75.0	N/A	N/A	1
	5.0	80	80.0	N/A	N/A	1
	10.0	83	83.0	N/A	N/A	1
	Overall		87.2	11.1	12.8	5
Wheat Straw	0.05	100, 84	92.0	11.3	12.3	2
	0.50	70	70.0	N/A	N/A	1
	5.0	89	89.0	N/A	N/A	1
	10.0	81	81.0	N/A	N/A	1
	Overall		84.8	11.0	13.0	5
Wheat Grain	0.05	94	94.0	N/A	N/A	1
	0.50	81	81.0	N/A	N/A	1
	5.0	93	93.0	N/A	N/A	1
	10.0	94	94.0	N/A	N/A	1
	Overall		90.5	6.4	7.0	4

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Table B.5.2.1-5: Recoveries of difenoconazole using AG-537A (but clean-up step with charcoal omitted).

Matrix	Fortification level [mg/kg]	Recoveries				N
		single values [%]	mean [%]	SD [%]	RSD dev. [%]	
Wheat Grain	0.05	76, 80	78.0	2.8	3.6	2
	0.25	73, 80	76.5	4.9	6.5	2
	Overall		77.3	3.4	4.4	4
Wheat Straw	0.05	112, 110	111.0	1.4	1.3	2
	0.25	90, 90	90.0	0.0	0.0	2
	Overall		100.5	12.2	12.1	4
Carrot	0.05	102	102.0	N/A	N/A	1
	0.25	92	92.0	N/A	N/A	1
	Overall		97.0	7.1	7.3	2

RMS comments: Method AG-537/537A is a valid and accurate method for the determination of difenoconazole residues in wheat. Validation/data complies mostly with the criteria in SANCO/3029/99 rev.4, 11/07/00. The method taken separately is not considered fully validated for carrot because the sample set is not complete. However, see also "Evaluation and assessment" (chapter B5.5).

Reference: Ross J. (1991). 'Analytical Method for the Determination of CGA-169374 in Wheat Raw Agricultural Commodities by Gas Chromatography with Nitrogen/Phosphorus Detection', Ciba-Geigy Corporation, Greensboro, USA, Unpublished report AG-575A. Syngenta File No. CGA169374/0450.

Method: **AG-575A**, pre-registration method. A representative crop sample is extracted by refluxing in 8:2 (v/v) methanol:conc. ammonium hydroxide. After filtering, an aliquot of the extract is diluted with water and saturated sodium chloride, and partitioned with hexane. The hexane fraction is partitioned with acetonitrile and the acetonitrile fraction is cleaned up on a silica gel Sep-Pak. The sample is then cleaned up on a phenyl Bond-elut, followed by a charcoal:magnesium oxide:celite column. The extract is analyzed by packed column gas chromatography using nitrogen/phosphorus detection.

GLP: Yes

Validation Data:

Specificity: No interferences were apparent at the retention time of the analyte of interest, indicating that the method is specific. Residues of difenoconazole in control samples were below the relevant limit of quantitation.

Linearity: Detector response was linear in the range 0.1-1 ng injected analyte; $r^2 = 0.99758$

Accuracy: All procedural recoveries were within the range 70-100% with a relative

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standard deviation of <20% (see table below)

Precision (Repeatability): Repeatability was within the requirements of EU-guidance ($RSD \leq 20\%$).

LOQ: 0.01 mg/kg

LOD: nd

Table B.5.2.1-6: Recoveries using AG-575 A (difenoconazole)

Matrix	Forti- fication Level [mg/kg]	Recoveries		SD [%]	RSD [%]	N
		single values [%]	mean [%]			
Wheat Grain	0.01	70, 85, 83, 79, 79, 89, 67, 88, 91	81.2	8.3	10.3	9
	0.05	83, 87, 70, 100, 102, 90	88.7	11.8	13.3	6
	0.10	109	109.0	N/A	N/A	1
	0.20	75	75.0	N/A	N/A	1
	1.0	97, 100, 78	91.7	11.9	13.0	3
	Overall		86.1	11.5	13.4	20
Wheat Straw	0.05	122	122	N/A	N/A	1
	0.075	85	85	N/A	N/A	1
	Overall		103.5	26.2	25.3	2
Wheat Forage	0.05	76	76.0	N/A	N/A	1
	Overall		76.0	N/A	N/A	1
Apple/Pear	0.01	95, 106, 107, 96, 77, 78, 108, 110, 79, 95, 102, 116, 89, 103, 77, 72, 75, 85, 99, 78, 73	91.4	14.1	15.5	21
	0.10	72, 103, 101, 118, 92, 73, 81, 74, 96, 72, 101, 106, 103, 105, 91, 89, 87, 83, 91, 75, 84	90.3	13.2	14.6	21
	0.30	86	86.0	N/A	N/A	1
	0.50	77, 92	84.5	10.6	12.6	2
	Overall		90.5	13.2	14.6	45
Carrots	0.01	88, 103, 88, 88, 91	91.6	6.5	7.1	5
	0.02	75, 70, 70	71.7	2.9	4.0	3
	0.1	83, 77, 83, 83, 78	80.8	3.0	3.8	5
	0.2	90, 85, 85	86.7	2.9	3.3	3
	Overall		83.6	8.4	10.0	16

RMS comments: Method AG-575A is a valid and accurate method for the determination of difenoconazole residues in wheat, apple/pears and carrot. Validation/data complies with the criteria in SANCO/3029/99 rev.4, 11/07/00.

Reference:

- Bussy L., Maffezzoni M. (1993).** 'Determination of CGA 169374 in vegetable matter, grapes and wine', Ciba-Geigy S.A., Unpublished report RES 10/93. Syngenta File No. CGA169374/0900.
- Ryan J (2004a).** 'Difenoconazole (CGA 169374): Summary of Validation Data for Analytical Method RES10/93 on Various Crops', Syngenta, Jealott's Hill International

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Method: Research Centre, UK, Unpublished report TMJ4940B. Syngenta File No. CGA169374/2421
RES 10/93, pre-registration method. The substance is extracted from the sample with methanol. After agitation, filtration and concentration, (the extract is diluted with water, partitioned methylene chloride then purified over basic aluminium oxide using ethyl ether as an eluant. The eluate is evaporated off and the residue dissolved in a hexane/ethanol mixture for determination by gas chromatography with an electron capture detector (GC-ECD).

GLP: 1. No; 2. No

Validation Data:

Specificity: No interferences were apparent at the retention time of the analyte of interest, indicating that the method is specific. Residues of difenoconazole in control samples were below the relevant limit of quantitation.

Linearity: Detector response was linear in the range 0.1-2 ng injected analyte; $r^2 = 0.9999$.

Accuracy: Overall mean recovery 110.2% (see table below), but 117.7% at one concentration level (outside 70-110%), incomplete sample set, $n < 10$.

Precision (Repeatability): Repeatability was within the requirements of EU-guidance ($RSD \leq 20\%$), but incomplete sample set, $n < 10$.

LOQ: 0.04 mg/kg (carrots)

LOD: nd

Results:

Table B.5.2.1-7: Recoveries of difenoconazole from carrot using RES 10/93

Matrix	Forti- fication level [mg/kg]	Recoveries single values [%]	Mean recoveries [%]	SD [%]	RSD [%]	N
Carrot	0.04	110, 113, 85	102.7	15.4	15.0	3
	0.20	112, 129, 112	117.7	9.8	8.3	3
	Overall		110.2	14.2	12.9	6

Table B.5.2.1-8: Overall recoveries from carrot, cauliflower, plum, peach and apricot using RES 10/93.

Matrix	Forti- fication level [mg/kg]	Recoveries range [%]	Mean recoveries [%]	RSD [%]	N
Carrot, cauliflower, plum, peach, apricot	0.04	76-118	97	113	14
	0.20	68-129	107	12	14
	Overall	68-129	102	13	28

RMS comments: Method RES 10/93 is considered a valid method for the determination of difenoconazole residues in carrot. The sample set is not completely fulfilled ($n=6 < 10$) but that is compensated for by additional

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data on similar high water content crops (see tables above). Further, recoveries also show some minor non-compliance, but that is also considered compensated for by the same additional data. Therefore, validation/data fulfil the criteria in SANCO/3029/99 rev.4, 11/07/00.

B.5.2.2 Analytical methods for analysis of residues in food of animal origin

Reference:	<p>1. Crook S.J. (2004). 'Residue Method for the Determination of Residues of Difenoconazole (CGA169374) and CGA 205375 in Animal Products. Final Determination by LC-MS/MS', Syngenta, Jealott's Hill International Research Centre, UK, Unpublished report REM 147.07. Syngenta File No. CGA205375/0021.</p> <p>2. Ryan J (2004b). 'Difenoconazole (CGA169374) and CGA205375: Validation of Residue Analytical Method REM 147.07 for the Determination of Residues in Animal Products', Syngenta, Jealott's Hill International Research Centre, UK, Unpublished report RJ3478B. Syngenta File No. CGA205375/0020.</p>
Method:	<p>REM 147.07, proposed as monitoring method. This analytical procedure is suitable for the determination of residues of difenoconazole and CGA205375 in animal products using an external standardization procedure.</p> <p>Samples are extracted by homogenization with acetonitrile:water (80:20 v/v). Extracts are centrifuged and aliquots (1 mL ~ 0.1 g) are diluted with ultra-pure water. Clean-up is performed by solid-phase extraction (SPE) using Oasis™ HLB cartridges. Final determination is by high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS).</p>
GLP:	<p>1. No.</p> <p>2. Yes.</p>
Validation Data:	
Specificity:	The MS/MS detection method is highly specific to the desired analytes with no interferences.
Linearity:	The detector response of difenoconazole and CGA205375 standards in mobile phase was shown to be linear through zero over a concentration range (n=5) of 0.000125 to 0.01 ug/ml (equivalent to 2.5 - 200 pg injected). r^2 (difenoconazole)=0.9998 and r^2 (CGA205375)=0.9997. No significant matrix effects on MS/MS detector response were observed for the matrices tested in this study.
Accuracy:	Determined as recovery (see table below). Acceptable mean recoveries of 70% to 110% were found for all matrices tested.
Precision (Repeatability):	RSD <20% (see table below).
LOQ:	0.01 mg/kg.
LOD:	nd.

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Results:**Table B.5.2.2-1: Recovery of Difenconazole from food of animal origin**

Matrix	Fortification Level (mg kg ⁻¹)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
Bovine Liver	0.01	95, 99, 100, 98, 98	98	2	95 - 100
	0.10	96, 93, 96, 95, 93	95	2	93 - 96
	Overall		96	2	93 - 100
Bovine Kidney	0.01	90, 98, 107, 100, 92	97	7	90 - 107
	0.10	91, 97, 92, 91, 93	93	3	91 - 97
	Overall		95	6	90 - 107
Bovine Muscle	0.01	94, 92, 96, 93, 95	94	2	92 - 96
	0.10	94, 93, 95, 96, 95	95	1	93 - 96
	Overall		94	1	92 - 96
Bovine Fat	0.01	99, 92, 97, 92, 89	94	4	89 - 99
	0.10	95, 96, 96, 97, 96	96	1	95 - 97
	Overall		95	3	89 - 99
Bovine Milk	0.005	96, 93, 99, 93, 101	96	4	93 - 101
	0.050	89, 86, 88, 85, 94	88	4	85 - 94
	Overall		92	6	85 - 101
Hen Eggs	0.01	90, 83, 92, 88, 79	86	6	79 - 92
	0.10	85, 79, 84, 82, 78	82	4	78 - 85
	Overall		84	6	78 - 92

Table B.5.2.2-2: Recovery of CGA 205375 (metabolite) from food of animal origin

Matrix	Fortification Level (mg kg ⁻¹)	Recovery (%)	Mean (%)	RSD (%)	Range (%)
Bovine Liver	0.01	99, 105, 95, 106, 92	99	6	92 - 106
	0.10	99, 94, 99, 100, 94	97	3	94 - 100
	Overall		98	5	92 - 100
Bovine Kidney	0.01	101, 104, 101, 106, 104	103	2	101 - 106
	0.10	91, 97, 94, 92, 91	93	3	91 - 97
	Overall		98	6	91 - 106
Bovine Muscle	0.01	90, 97, 91, 89, 98	93	4	89 - 97
	0.10	91, 95, 97, 100, 97	96	3	91 - 100
	Overall		95	4	89 - 100
Bovine Fat	0.01	92, 97, 93, 92, 95	94	2	92 - 97
	0.10	97, 94, 93, 99, 93	95	3	93 - 99
	Overall		95	3	92 - 99
Bovine Milk	0.005	92, 92, 107, 90, 102	97	8	90 - 107
	0.05	88, 90, 92, 89, 91	90	2	88 - 92
	Overall		93	7	88 - 107
Hen Eggs	0.01	90, 82, 88, 86, 92	88	4	82 - 92
	0.10	89, 85, 89, 88, 82	87	4	82 - 89
	Overall		87	4	82 - 92

RMS comments: The method is considered valid for the determination of difenoconazole and CGA 205375 residues in animal products at the LOQ and over the concentration ranges typical of that for which the method will be used (validation/data complies with the criteria in SANCO/825/00 rev. 7, 17/03/2004), see also Independent Laboratory Validation (next), and "Evaluation and assessment" (chapter B5.5).

Independent Laboratory Validation

Reference: Benaseraf L. (2004). 'Inter-Laboratory Validation of Residue Method REM 147.07 for

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the Determination Of Difenoconazole In Hen Egg, Bovine Milk and Bovine Muscle', ADME Bioanalyses, Unpublished report SYN/DIF/04031. Syngenta File No. CGA169374/2535.

Method: See above.

GLP: Yes.

Validation Data:

Specificity: The MS/MS detection method is highly specific to the desired analytes with no interferences.

Linearity: The detector response of difenoconazole and CGA205375 in matrix standards was shown to be linear in the concentration range (n=6) of 0.00025 to 0.006 ug/ml. r^2 (difenoconazole) were in range 0.9975-0.9993 and r^2 (CGA205375) in the range 0.9952-0.9996.

Accuracy: Determined as recovery (se table below). All procedural recoveries were within the range 70-110%.

Precision (Repeatability): Determined as RSD (se table below). All RSD were < 20%.

LOQ: 0.01 mg/kg (bovine muscle, milk and hen eggs).

LOD: nd.

Results:

Table B.5.2.2-3: Recovery of Difenoconazole from food of animal origin (ILV report)

Matrix	Fortification Level (mg kg ⁻¹)	Recovery (%)	n	Mean (%)	RSD (%)	Range
Hen egg	Control	ND, ND	2			
	0.01*	110, 101, 84, 103, 85	5	97	12	84 - 110
	0.1	97, 94, 94, 95, 100	5	96	3	94 - 100
	Overall		10	96	8	84 - 110
Bovine milk	Control	ND, ND	2			
	0.005*	72, 62, 81, 84, 84	5	77	12	62 - 84
	0.05	89, 86, 92, 91, 87	5	89	3	86 - 92
	Overall		10	83	11	62 - 92
Bovine muscle	Control	ND, ND	2			
	0.01*	72, 99, 93, 97, 100	5	92	13	72 - 100
	0.1	94, 96, 101, 100, 91	5	96	4	91 - 101
	Overall		10	94	9	72 - 101

*Limit of quantification (LOQ), defined by the lowest validated fortification level

ND : Non-detectable residue < 30% LOQ

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Table B.5.2.2-4: Recovery of CGA 205375 (metabolite) from food of animal origin (ILV report)

Matrix	Fortification Level (mg kg ⁻¹)	Recovery (%)	n	Mean (%)	RSD (%)	Range
Hen egg	Control	ND, ND	2			
	0.01*	94, 98, 105, 104, 109	5	102	6	94 - 109
	0.1	101, 94, 99, 100, 99	5	99	3	94 - 101
	Overall		10	100	5	94 - 109
Bovine milk	Control	ND, ND	2			
	0.005*	92, 101, 98, 110, 88	5	98	9	88 - 110
	0.05	93, 89, 92, 89, 89	5	90	2	89 - 93
	Overall		10	94	7	88 - 110
Bovine muscle	Control	ND, ND	2			
	0.01*	97, 110, 103, 98, 96	5	101	6	96 - 110
	0.1	99, 98, 99, 97, 99	5	98	1	97 - 99
	Overall		10	100	4	96 - 110

*Limit of quantification (LOQ), defined by the lowest validated fortification level

ND : Non-detectable residue < 30% LOQ

RMS comments: The independent laboratory validation of this method shows that it is suitable for use as a monitoring method (validation/data complies with the criteria in SANCO/825/00 rev. 7, 17/03/2004).

Reference: **Steinhauer S. (2004b),** 'Difenoconazole: Validation of the DFG Method S 19 (Extended Revision) for the Determination of Residues of Difenoconazole in Milk, Meat, Fat, Egg, Liver and Kidney', Dr Specht & Partner Chem. Laboratorien GmbH. Unpublished Report No. SYN-0302V Az. G03-0024, Syngenta File No. 2443.

Method: **The DFG Method S 19** (extended revision), was tested for use as a monitoring method for determination of the residues of difenoconazole in milk, meat, egg, liver, kidney and fat. However, the notifier found that they could not recommend the method for this application. Data are presented here only for general interest.

The extractions of the pesticide (see also corresponding application to crops) from the matrices were performed according to extraction modules E1 (milk, meat, egg, liver and kidney) as well as E7 (fat) followed by clean-up procedures according to module GPC and module C1 (silica gel mini column). The primary detection technique was capillary gas chromatography with nitrogen phosphorus detection (NPD, module D3). A confirmatory technique of GC with mass spectrometric detection (MSD, module D4) at mass to charge ratio of $m/z = 325$ for quantitation was tested. Finally, high performance liquid chromatography using tandem mass spectrometric detection was used for quantitation of Difenoconazole using mass transition m/z 406 → 251 for all matrices.

GLP: Yes

Validation data: Tables below

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Table B.5.2.2-5: Average % recoveries obtained using capillary gas chromatography with nitrogen phosphorus detection (GC-NPD)

Matrix	Forti- fication level (mg/kg)	Recoveries				N
		single values [%]	mean [%]	SD [%]	RSD [%]	
Milk	0.02	99, 96, 103, 100, 89	97	5.3	5.5	5
	0.2	94, 110, 107, 108, 108	105	6.5	6.2	5
	Overall		101	7.0	6.9	10
Meat	0.02	91, 106, 116, 108, 110	106	9.3	8.8	5
	0.2	99, 101, 106, 83, 99	98	8.6	8.8	5
	Overall		102	9.6	9.4	10
Egg	0.05	103, 111, 98, 102, 113	105	6.3	6.0	5
	0.5	95, 113, 112, 116, 110	109	8.2	7.5	5
	Overall		107	7.2	6.7	10
Fat	0.05	102, 95, 101, 108, 101	101	4.6	4.6	5
	0.5	93, 95, 110, 108, 103	102	7.6	7.5	5
	Overall		102	5.9	5.8	10

Table B.5.2.2-6: Average % recoveries obtained using high performance liquid chromatography using tandem mass spectrometric detection (LC-MS/MS)

Matrix	Forti- fication level [mg/kg]	Recoveries				N
		single values [%]	mean [%]	SD [%]	RSD [%]	
Milk	0.02	100, 99, 108, 106, 101	102.8	4.0	3.9	5
	0.2	110, 120, 122, 120, 124	119.2	5.4	4.5	5
	Overall		111.0	9.7	8.8	10
Meat	0.02	144, 124, 126, 128, 131	130.6	7.9	6.1	5
	0.2	150, 122, 127, 108, 133	128.0	15.4	12.0	5
	Overall		129.3	11.6	9.0	10
Egg	0.05	116, 122, 117, 103, 105	112.6	8.2	7.3	5
	0.5	109, 117, 121, 123, 116	117.2	5.4	4.6	5
	Overall		114.9	7.0	6.1	10
Fat	0.02	97, 95, 92, 93, 97	94.8	2.3	2.4	5
	0.2	91, 96, 78, 95, 95	91.0	7.5	8.3	5
	Overall		92.9	5.6	6.0	10
Liver	0.02	104, 108, 115, 112, 118	111.4	5.5	5.0	5
	0.2	104, 111, 117, 95, 110	107.4	8.3	7.8	5

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Matrix	Forti- fication level [mg/kg]	Recoveries				N
		single values [%]	mean [%]	SD [%]	RSD [%]	
	Overall		109.4	7.0	6.4	10
Kidney	0.02	126, 116, 125, 128, 111	121.2	7.3	6.0	5
	0.2	121, 91, 119, 114, 121	113.2	12.7	11.3	5
	Overall		117.2	10.7	9.1	10

RMS comments: The average percent recoveries obtained using capillary gas chromatography with nitrogen phosphorus detection (NPD) are shown in Table 4.2.1.2-12 above.

The results of the confirmatory method with mass selective detection module D4 (MSD) resulted in recovery values above 110%. The confirmatory method proves unequivocally the peak identity but did not demonstrate the principle applicability of the DFG Method S 19 for the determination of Difenoconazole residues in materials of the above-mentioned animal origin.

Analysis of control specimens of milk, meat, egg, liver, kidney and fat by LC-MS/MS yielded no residues of Difenoconazole above the limit of detection after extraction modules E 1 or E 7 and gel permeation chromatography (GPC) and silica gel mini column (module C 1), indicating that no interferences were present at the retention time of Difenoconazole in the test system. The average percent recoveries obtained using high performance liquid chromatography using tandem mass spectrometric detection (LC-MS/MS) are shown in Table 4.2.1.2-13 above. Mean recovery values obtained by LC-MS/MS for milk, meat, egg, liver, kidney and fat for both fortification levels (LOQ and ten times LOQ) do not comply with the standard acceptance criteria of SANCO Guideline 825/00, which demand that the mean recovery at each fortification level should be in the range of 70-110%.

It is therefore concluded, that the enforcement method DFG Method S 19 (extended revision) has not proven its applicability for the determination of difenoconazole in milk, meat, egg, liver, kidney and fat, due to the fact that confirmatory method GC-MSD failed and LC-MS/MS detection resulted in mean recoveries values above the 110% level for milk, meat, egg and kidney. This result means that this method is not recommended for monitoring residues in products of animal origin; instead it is proposed that method REM 147.07 should be used, which has been successfully validated in an independent laboratory.

Reference:

Wurz R.E.M. (1994). 'Analytical method for the determination of CGA 169374 residues in dairy and poultry tissue, eggs and milk by gas chromatography', Ciba-Geigy Corp., Greensboro NC, USA, Unpublished report AG-544A. Syngenta File No. CGA169374/0933

Method:

AG-544A, pre-registration method. A representative sample is extracted by homogenizing with 95:5 (v/v) acetonitrile:conc. ammonium hydroxide. After filtering, an aliquot of the extract is diluted with water and saturated sodium chloride and partitioned with hexane. The hexane fraction is partitioned with acetonitrile and the acetonitrile fraction is cleaned up on a silica gel SepPak. The final extract is analyzed by packed column gas chromatography using alkali flame ionization detection.

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Modifications: Blood and milk were shaken instead of maceration. Replicate analysis of milk specimens of sampling days 1 and 7 Apr 1999 were done by maceration. The fat was melted and shaken with the same solvent instead of cold maceration. For the re-extraction (section 3.0) tert-butylmethyl ether had to be used instead of hexane, to extract both analytes (parent and metabolite). Section 4.0 was not performed. Final quantitation was by LC-MS-MS using mass transition m/z 406 -> 251.

GLP: No

Validation Data:

Specificity: Demonstrated using GC-NPD as the analyte had the same retention time as the certified standard, with no interferences evident at that retention time.

Linearity: The detector response was linear in the range 0.20 – 10 ng injected; $r = 0.999968$

Accuracy: Mean recoveries for milk ranging from 111.0-118.0%, which is slightly outside upper acceptable limit 110%. All other mean recoveries were in the range 70-110%, see table below.

Precision (Repeatability): Repeatability was within the requirements of EU-guidance ($RSD \leq 20\%$), see table below.

LOQ: 0.01 mg/kg (milk), 0.05 mg/kg (muscle, fat, liver, kidney, eggs). Sample set for LOQ of milk not complete ($n=2<5$).

LOD: nd

Results:

Table B.5.2.2-5: Recoveries of Difenconazole from animal products using AG 544A

Matrix	Forti- fication level [mg/kg]	Recoveries single values [%]	Mean recoveries [%]	SD [%]	RSD [%]	N
Milk	0.01	34, 102	118.0	22.6	19.2	2
	0.05	118	118.0	N/A	N/A	1
	0.50	111	111.0	N/A	N/A	1
	Overall		116.3	13.5	11.6	4
Muscle	0.05	110, 110, 108, 108, 76, 91	100.5	14.0	14.0	6
	0.10	99, 104, 91	98.0	6.6	6.7	3
	0.50	96, 99, 86	93.7	6.8	7.3	3
	Overall		98.2	10.7	10.9	12
Fat	0.05	95, 108, 81, 91, 103, 103	96.8	9.9	10.2	6
	0.10	97, 98, 98	97.7	0.6	0.6	3
	0.50	95, 94, 110	99.7	9.0	9.0	3
	Overall		97.8	7.8	8.0	12
Liver	0.05	121, 121, 97, 97	109.0	13.9	12.7	4
	0.10	109, 92	100.5	12.0	12.0	2
	0.50	109, 91	100.0	12.7	12.7	2
	Overall		104.6	12.2	11.6	8
Kidney	0.05	89, 89	89.0	0.0	0.0	2
	0.10	96	96.0	N/A	N/A	1
	0.50	102	102.0	N/A	N/A	1

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Matrix	Forti- fication level [mg/kg]	Recoveries single values [%]	Mean recoveries [%]	SD [%]	RSD [%]	N
Eggs	Overall		94.0	6.3	6.7	4
	0.05	74, 81	77.5	4.9	6.4	2
	0.10	81	81.0	N/A	N/A	
	0.50	83	83.0	N/A	N/A	1
	Overall		79.8	3.9	4.9	4

RMS comments: Method AG-544A is considered a valid and accurate method for the determination of difenoconazole residues in muscle, fat and liver. Validation/data complies mostly with the criteria in SANCO/3029/99 rev.4, 11/07/00 for these matrices. The method is not considered fully validated for milk, kidney and eggs because the sample set is incomplete and accuracy also show some non-compliances, but of minor importance. See also "Evaluation and assessment" (chapter B5.5).

Reference: **Tribolet, R. (2000)**, 'Residue of Difenoconazole (CGA 169374) and its Metabolite CGA 205375 in Milk, Blood and Tissues (Muscle, Fat, Liver, Kidney) of Dairy Cattle Resulting From Feeding of Difenoconazole at Three Dose Levels', Novartis Crop Protection AG, Basel, Switzerland. Unpublished Report 202/99, SAM No. 2039. Study dates 10.3.99 to 29.5.2000.

Method: **AG 544A** modified, a pre-registration method, see above

GLP: Yes

Validation Data:

Specificity: Quantitation is by LC-MS/MS, which is a highly specific detection technique.

Linearity: Detector responses were linear. Difenoconazole: range 2-50 ng/ml, s=1.6%. CGA 205375: range 2-50 ng/ml, s=1.6%. Five conc. levels.

Accuracy: Recoveries for both difenoconazole and CGA 205375 were in the range 70-110% (see tables below), n<10 several cases (formal validation)

Precision (Repeatability): Repeatability was within the requirements of EU-guidance ($RSD \leq 20\%$), apart from difenoconazole in muscle and CGA 205375 in kidney, which were only marginally outside this range at 21 and 23% respectively (see tables below), n<10 several cases (formal validation).

LOQ: 0.01 mg/kg (liver, kidney, muscle, fat; n<5), 10 ug/l (blood; n<10), 5 ug/l (milk).

LOD: nd

Results:

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Table B.5.2.2-5: Recoveries of Difenconazole from animal products using modified version of AG-544A

Matrix	Fortification level	Recoveries single values [%]	Mean recoveries [%]	SD [%]	RSD [%]	N
Liver	0.01 [mg/kg]	68, 78	73.0	7.1	9.7	2
	0.1 [mg/kg]	80	80.0	N/A	N/A	1
	0.2 [mg/kg]	72	72.0	N/A	N/A	1
	Overall		74.5	5.5	7.4	4
Kidney	0.01 [mg/kg]	83, 76	79.5	4.9	6.2	2
	0.1 [mg/kg]	81	81.0	N/A	N/A	1
	Overall		80.0	3.6	4.5	3
Muscle	0.01 [mg/kg]	73, 86, 120	93.0	24.3	26.1	3
	0.1 [mg/kg]	76, 73, 86	78.3	6.8	8.7	3
	Overall		85.7	17.9	20.8	6
Fat	0.01 [mg/kg]	86, 77	81.5	6.4	7.8	2
	0.1 [mg/kg]	79, 78	78.5	0.7	0.9	2
	Overall		80.0	4.1	5.1	4
Blood	10 [mg/l]	84, 84	84.0	0.0	0.0	2
	100 [mg/l]	79, 80	79.5	0.7	0.9	2
	Overall		81.8	2.6	3.2	4
Milk	5 [mg/l]	94, 98, 91, 86, 90, 80, 78, 79, 90	87.3	7.1	8.1	9
	50 [mg/l]	87, 91, 84, 86, 78, 84, 78, 78, 87	83.7	4.7	5.6	9
	Overall		85.5	6.1	7.2	18

Table B.5.2.2-6: Recoveries of CGA 205375 (metabolite) from animal products using modified version of AG-544A

Matrix	Fortification level	Recoveries single values [%]	Mean recoveries [%]	SD [%]	RSD [%]	N
Liver	0.01 [mg/kg]	84, 117	100.5	23.2	23.2	2
	0.1 [mg/kg]	85, 89	87.0	2.8	3.3	2
	0.2 [mg/kg]	88	88.0	N/A	N/A	1
	Overall		92.6	13.8	14.9	5
Kidney	0.01 [mg/kg]	113, 73	93.0	28.3	30.4	2
	0.1 [mg/kg]	83	83.0	N/A	N/A	1
	Overall		89.7	20.8	23.2	3
Muscle	0.01 [mg/kg]	97, 103, 97	99.0	3.5	3.5	3
	0.1 [mg/kg]	102, 76, 92	90.0	13.1	14.6	3
	Overall		94.5	9.9	10.5	6
Fat	0.01 [mg/kg]	83, 93, 73	83.0	10.0	12.0	3
	0.1 [mg/kg]	83, 79	81.0	2.8	3.5	2
	Overall		82.2	7.3	8.9	5
Blood	10 [mg/l]	83, 84	83.5	0.7	0.8	2
	100 [mg/l]	80, 81	80.5	0.7	0.9	2
	Overall		82.0	1.8	2.2	4
Milk	5 [mg/l]	100, 94, 102, 99, 93, 84, 73, 80, 93, 93	91.3	9.3	10.2	10
	50 [mg/l]	97, 99, 99, 97, 84, 87, 73, 74, 80, 86	87.6	10.0	11.5	10
	Overall		89.4	9.6	10.7	20

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Table B.5.2.2-7: Supporting recoveries of Difenconazole from animal products using modified AG 544A (storage stability data)

Matrix	Fortification Level	Recovery Single Values [%]	Mean Recoveries	SD [%]	RSD [%]	N
Muscle	0.2 (mg/kg)	85, 85, 95, 85, 85	87	4	5	5
Liver	0.2 (mg/kg)	70, 75, 50, 65, 65	65	9	14	5
Kidney	0.2 (mg/kg)	75, 75, 45, 55, 65	63	13	21	5
Fat	0.2 (mg/kg)	80, 75, 70, 80, 85	78	6	7	5
Milk	50 (µg/l)	80, 78, 80, 82, 78	80	2	2	5
Blood	100 (µg/l)	85, 83, 81, 83, 83	83	1	2	5

Table B.5.2.2-8: Supporting recoveries of CGA205375 (metabolite) from animal products using modified AG 544A (storage stability data)

Matrix	Fortification Level	Recovery Single Values [%]	Mean Recoveries	SD [%]	RSD [%]	N
Muscle	0.2 (mg/kg)	80, 85, 90, 90, 75	84	7	8	5
Liver	0.2 (mg/kg)	90, 90, 90, 95, 85	90	4	4	5
Kidney	0.2 (mg/kg)	70, 85, 80, 65, 70	74	8	11	5
Fat	0.2 (mg/kg)	85, 80, 80, 85, 80	82	3	3	5
Milk	50 (µg/l)	78, 74, 72, 74, 78	75	3	4	5
Blood	100 (µg/l)	86, 88, 88, 84, 87	87	2	2	5

RMS comments: Method AG-544A modified version is considered a valid and accurate method for the determination of residues of difenconazole and CGA 205375 in the tested matrices if supporting data are also considered. Validation/data complies with the criteria in SANCO/3029/99 rev.4, 11/07/00, with only a few non-compliances of minor importance. However, regarding method AG-544A (modified) it should be noted that although the method/validation is considered generally acceptable the LOQ is somewhat uncertain for all matrices except milk (due to incomplete dataset at that level). See also "Evaluation and assessment" (chapter B5.5).

B.5.3 Analytical methods (residue) soil, water, air (Annex IIA 4.2.2 to 4.2.4; Annex IIIA 5.2)

B.5.3.1 Analytical method for the determination of residues in soil

Reference:	Tummon O.J. (2004a). Validation of an analytical method for the determination of difenoconazole and CGA 205375 in soil. Syngenta, Jealott's Hill International Research Centre, Bracknell, UK. Unpublished Report No. RJ3459B. Issue date: 21 April 2004, Syngenta File No. CGA169374/2501.
Method:	RAM 421/01 , proposed as a monitoring method: A 10 g sub sample of soil is extracted by reflux with methanol/ammonia solution (80:20, v/v) for two hours. After centrifugation, an aliquot of the soil extract is evaporated to dryness and re-dissolved in acetonitrile/water solution (30:70, v/v) prior to analysis by high performance liquid chromatography with triple quadrupole mass spectrometry detection (LC-MS/MS). The limit of quantification of the method is 0.01 mg kg ⁻¹ .
GLP:	Yes.
Validation Data:	
Specificity:	LC-MS/MS is a highly specific quantification technique with negligible interference from the soil matrices. Residues of difenoconazole and CGA 205375 in the control samples were less than 30% of the LOQ. A confirmatory technique is not required.
Linearity:	Linearity of detector response for difenoconazole and CGA 205375 was demonstrated over the concentration range 0.0001 µg/ml – 0.01 µg/ml (equivalent to the range of injected analyte amount of 5 pg – 500 pg with a 50 µL injection volume); $r^2 = 0.9940$ to 0.9973).
Accuracy:	The accuracy, as determined by procedural recoveries at fortification levels from 0.01 – 0.1 mg/kg were between 70% and 110%.
Precision (Repeatability):	Precision under repeatability conditions was within the requirements of EU-guidance ($RSD \leq 20\%$).
LOQ:	0.01 mg/kg for both difenoconazole and CGA 205375 in soil. It is below the proposed limit of quantification by SANCO/3029/rev.4, i.e. it does not exceed 0.05 mg/kg in soil.
LOD:	LOD for both analytes was estimated to be 0.001 mg/kg.
Results:	

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Table 5.3.1-1: Recovery of Difenoconazole from soil

Matrix	Fortification Level (mg kg ⁻¹)	Recovery (%)**	Mean (%)	RSD (%)	Range (%)
Sandy Loam Soil (Pappelacker Soil)	0.01 *	104,96,100,93,91	97	5	91-104
	0.10	82,100,94,99,83	92	9	82-100
		Overall	95	7	82-104
Silty Clay Loam Soil (Scheueracker soil)	0.01 *	95,81,89,86,89	88	5	81-95
	0.10	95,78,80,93,75	84	9	75-95
		Overall	86	7	75-95

* Limit of quantification, defined by the lowest validated fortification level

** Residues in control samples were less than 30% of the LOQ. Two controls per soil type were analysed.

Table 5.3.1-2: Recovery of CGA 205375 (metabolite) from soil

Matrix	Fortification Level (mg kg ⁻¹)	Recovery (%)**	Mean (%)	RSD (%)	Range (%)
Sandy Loam Soil (Pappelacker Soil)	0.01 *	103,89,101,109,104	101	7	89-109
	0.10	89,102,100,106,105	100	7	89-106
		Overall	101	7	89-109
Silty Clay Loam Soil (Scheueracker soil)	0.01 *	101,88,107,105,106	101	8	88-107
	0.10	89,80,84,105,87	89	10	80-105
		Overall	95	9	80-107

* Limit of quantification, defined by the lowest validated fortification level

** Residues in control samples were less than 30% of the LOQ. Two controls per soil type were analysed.

RMS comments: Method RAM 421/01 is suitable for monitoring residues of difenoconazole and CGA 205375 in soil. Validation/data complies with SANCO/825/00 rev. 7, 17/03/2004.

Reference:

1. **Williams R.K. (1986).** Analytical method for the determination of CGA 169374 in soil by gas chromatography. Ciba-Geigy Corp., Greensboro, United States. Unpublished Report No. AG-501. Issue date: August 1986 (Syngenta File No. CGA169374/0051).
2. **Kühne-Thu H. (1990a).** Determination of residues of parent compound in soil after treatment with fungicide 'CGA169374 EC 250'. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. 2023/89 Issue date: September 1990 (Syngenta File No. CGA169374/0342).
3. **Kühne-Thu H. (1990b).** Determination of residues of parent compound in soil after treatment with fungicide 'CGA169374 EC 250'. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. 2024/89 Issue date: September 1990 (Syngenta File No. CGA169374/0341).

Method:

AG-501, proposed as a monitoring method. A soil sample is extracted by refluxing in methanol/concentrated aqueous ammonium hydroxide (8 vol. + 2 vol.) for two hours. After filtration, an aliquot of the extract is diluted with water and saturated sodium

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chloride solution. The diluted extract is partitioned with n-hexane or dichloromethane. The combined fractions are evaporated to dryness.

An optional clean-up step (omitted in most cases) can be carried out using a silica gel Sep-Pak cartridge or equivalent. The final eluate is evaporated to dryness. The residue is dissolved in toluene. The final determination of the resulting solution is performed by packed column gas chromatography using alkali flame ionization detection (AFID; Nitrogen-Phosphorus detector (NPD)).

Modified version: See below.

GLP: Method validation: No. Field trials: Yes

Validation Data:

Specificity: GC-NPD is a specific quantification technique and allows the separation of the analyte from interferences. Residues of difenoconazole in the control samples were below LOQ. Method RAM 421/01 could be used for confirmation (LC-MS/MS).

Linearity: Linearity of detector response for difenoconazole (GC-NPD) was demonstrated over the concentration range 0.02 µg/ml – 1.0 µg/ml (equivalent to the range of injected analyte amount of 0.04 ng – 2.0 ng with 2 µL injection volume; $r^2 = 0.9991$).

Accuracy: The accuracy, as determined by mean recoveries at fortification levels from 0.05 – 1.0 mg/kg ranged from 87% to 117% (overall mean: 105%; N=30) with individual recoveries ranging from 82 – 134%. Only one set of values (i.e. Everglades Peat with 116%) was outside to 70% – 110% range. See summary table below.

Precision (Repeatability): Precision under repeatability conditions was within the requirements of EU-guidance (RSD ≤ 20%).

LOQ: 0.05 mg/kg for soil (at this fortification level, the corresponding mean recovery was between 70% and 110% and RSD was ≤ 20%). It does not exceed the proposed limit of quantification by SANCO/3029/rev.4, i.e. it does not exceed 0.05 mg/kg in soil.

LOD: nd

RMS comments: Method AG-501 is a valid and accurate monitoring method for the determination of difenoconazole residues in soil. Validation/data complies with the criteria in SANCO/825/00 rev. 7, 17/03/2004, except some minor deviations.

Reference: See AG-501 above

Method: **AG-501 modified**, proposed as a monitoring method. Modified version of method AG-501, see above. For the analysis of samples from field studies some minor modifications were made: The silica Sep-Pak clean-up step was partly omitted and the final determination was made with by gas chromatography using electron capture detection (ECD).

GLP: see above.

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Validation Data:

Specificity:	GC-ECD is a specific quantification technique and allows the separation of the analyte from interferences. Residues of difenoconazole in the control samples were below LOQ. Method RAM 421/01 could be used for confirmation (LC-MS/MS).
Linearity:	Linearity of detector response for difenoconazole (GC-ECD) was demonstrated over the concentration range 0.02 µg/ml – 0.5 µg/ml (equivalent to the range of injected analyte amount of 0.04 ng – 1.0 ng with 2 µL injection volume; $r^2 = 0.9907$).
Accuracy:	The accuracy, as determined by mean recoveries at fortification levels from 0.04 – 0.2 mg/kg ranged from 109% to 112% (overall mean: 111%; N=8) with individual recoveries ranging from 101 – 119% (see summary table below).
Precision (Repeatability):	Precision under repeatability conditions was within the requirements of EU-guidance ($RSD \leq 20\%$).
LOQ:	0.04 mg/kg for soil (at this fortification level, the corresponding mean recovery (112%) was only slightly higher than 110% and $RSD \leq 20\%$). it is below the proposed limit of quantification by SANCO/3029/rev.4, i.e. it does not exceed 0.05 mg/kg in soil.
LOD:	nd

RMS comments: Method AG-501 modified version is a valid and accurate monitoring method for the determination of difenoconazole residues in soil. Validation/data complies with the criteria in SANCO/825/00 rev. 7, 17/03/2004, except some minor deviations.

Reference:

- 1. Williams, R.K. Shoffner, K.P. (1987).** Analytical method for the determination of CGA 169374 in tomatoes and potatoes by gas chromatography. Ciba-Geigy Corp., Greensboro, United States. Unpublished Report No. AG-514 Issue date: March 1987(Syngenta File No. CGA169374/0052).
- 2. Kühne-Thu H. (2000).** Long term study on fate and behaviour of Difenoconazole (CGA 169374) in soil in Switzerland. Novartis Crop Protection AG, Basel, Switzerland. Unpublished Report No. 2031/89-98 Issue date: April 2000(Syngenta File No. CGA169374/0652).
- 3. Kühne-Thu H. (1990c).** Determination of residues of parent compound in soil after treatment with 'Difenoconazole EC 250' – field experiment. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. 2097/89 Issue date: November 1990(Syngenta File No. CGA169374/0335)
- 4. Kühne-Thu H. (1990d).** Determination of residues of parent compound in soil after treatment with 'Difenoconazole EC 250' – field experiment. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. 2096/89 Issue date: November 1990(Syngenta File No. CGA169374/0336)
- 5. Kühne-Thu H (1991a).** Determination of residues of parent compound in soil after treatment with 'Difenoconazole EC 250' – field experiment. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. 2040/89 Issue date: January 1991(Syngenta File No. CGA169374/0337).
- 6. Kühne-Thu H (1991b).** Determination of residues of parent compound in soil after treatment with 'Difenoconazole EC 250' – field experiment. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. 2039/89 Issue date: January 1991(Syngenta File No. CGA169374/0338).
- 7. Kühne-Thu H (1990b).** Determination of residues of parent compound in soil after treatment with fungicide 'CGA169374 EC 250'. Ciba-Geigy Ltd., Basel, Switzerland.

	<p>Unpublished Report No. 2024/89 Issue date: September 1990(Syngenta File No. CGA169374/0341).</p> <p>8. Kühne-Thu H (1990a). Determination of residues of parent compound in soil after treatment with fungicide 'CGA169374 EC 250'. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. 2023/89 Issue date: September 1990(Syngenta File No. CGA169374/0342).</p>
Method:	<p>AG-514, modified for soil analyses, proposed as a monitoring method: A soil sample is extracted by refluxing in methanol/concentrated aqueous ammonium hydroxide (8 vol. + 2 vol.) for two hours.</p> <p>After cooling down to room temperature, an aliquot of the extract is diluted with water and saturated sodium chloride solution. The diluted extract is partitioned with n-hexane or dichloromethane. The combined hexane fractions are evaporated to dryness.</p> <p>An optional clean-up step (omitted in most cases) can be carried out using a silica gel Sep-Pak cartridge or equivalent. The final eluate is evaporated to dryness. The residue is dissolved in toluene. The final determination of the resulting solution is performed by gas chromatography using electron capture detection (ECD).</p>
GLP:	No
Validation Data:	
Specificity:	GC-ECD is a specific quantification technique and allows the separation of the analyte from interferences. Residues of difenoconazole in the control samples were below LOQ. Method RAM 421/01 could be used for confirmation (LC-MS/MS).
Linearity:	Linearity of detector response for difenoconazole (GC-ECD) was demonstrated over the concentration range 0.02 µg/ml – 0.25 µg/ml (equivalent to the range of injected analyte amount of 0.04 ng – 0.5 ng with 2 µL injection volume; $r^2 = 0.9874$).
Accuracy:	The accuracy, as determined by mean recoveries at fortification levels from 0.04 – 0.2 mg/kg ranged from 105% to 106% (overall mean: 105%; N=34) with individual recoveries ranging from 87 – 122% (see summary table below).
Precision (Repeatability):	Precision under repeatability conditions was within the requirements of EU-guidance ($RSD \leq 20\%$).
LOQ:	0.04 mg/kg for soil (at this fortification level, the corresponding mean recovery was between 70% and 110% and RSD was $\leq 20\%$). It is below the proposed limit of quantification by SANCO/3029/rev.4, i.e. it does not exceed 0.05 mg/kg in soil.
LOD:	nd
RMS comments:	Method AG-514 modified for soil analysis is a valid and accurate monitoring method for the determination of difenoconazole residues in soil. Validation/data complies with the criteria in SANCO/825/00 rev. 7, 17/03/2004.
Reference:	1. Ross, J. (1991). Analytical method for the determination of CGA 169374 in wheat raw agricultural commodities by gas chromatography with nitrogen/phosphorus detection.

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	<p>Ciba-Geigy Corp., Greensboro, United States. Unpublished Report No. AG-575A Issue date: May 1991 (Syngenta File No. CGA169374/0450).</p> <p>2. Kühne-Thu H. (2000). Long term study on fate and behaviour of Difenconazole (CGA 169374) in soil in Switzerland. Novartis Crop Protection AG, Basel, Switzerland. Unpublished Report No. 2031/89-98 Issue date: April 2000 (Syngenta File No. CGA169374/0652).</p> <p>3. Kühne-Thu H. (1992). Determination of residues of difenoconazole in asparagus and soil – field trial. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. 2056/89 Issue date: August 1992 (Syngenta File No. CGA169374/0695).</p>
Method:	<p>AG-575A, modified for soil analyses, proposed as a monitoring method: A soil sample is extracted by refluxing in methanol/concentrated aqueous ammonium hydroxide (8 vol. + 2 vol.) for two hours.</p> <p>After cooling down to room temperature, an aliquot of the extract is diluted with water and saturated sodium chloride solution. The diluted extract is partitioned twice with n-hexane. The combined hexane fractions are evaporated to dryness.</p> <p>An optional clean-up step (omitted in most cases) can be carried out using a silica gel Sep-Pak cartridge or equivalent. The final eluate is evaporated to dryness. The residue is dissolved in toluene. The final determination of the resulting solution is performed by gas chromatography using electron capture detection (ECD).</p>
GLP:	1. Yes; 2. Yes; 3. Yes.
Validation Data:	
Specificity:	GC-ECD is a specific quantification technique and allows the separation of the analyte from interferences. Residues of difenoconazole in the control samples were below LOQ. Method RAM 421/01 could be used for confirmation (LC-MS/MS).
Linearity:	Linearity of detector response for difenoconazole (GC-NPD) was demonstrated over the concentration range 0.02 µg/ml – 0.2 µg/ml (equivalent to the range of injected analyte amount of 0.04 ng – 0.4 ng with 2 µL injection volume; $r^2 = 0.9977$).
Accuracy:	The accuracy, as determined by mean recoveries at fortification levels from 0.02 – 0.7 mg/kg ranged from 93% to 105% (overall mean: 101%; N=14) with individual recoveries ranging from 85 – 115% (see summary table below).
Precision (Repeatability):	Precision under repeatability conditions was within the requirements of EU-guidance (RSD ≤ 20%).
LOQ:	0.02 mg/kg for soil (at this fortification level, the corresponding mean recovery was between 70% and 110% and RSD was ≤ 20%). It is below the proposed limit of quantification by SANCO/3029/rev.4, i.e. it does not exceed 0.05 mg/kg in soil.
LOD:	nd

RMS comments: Method AG-575A modified for soil analysis is a valid and accurate monitoring method for the determination of difenoconazole residues in soil. Validation/data complies with the criteria in SANCO/825/00 rev. 7-17/03/2004.

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Reference:	<p>1. Kühne-Thu H. (1986). Determination of parent compound by gas chromatography. Plant material. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. REM 7/86 Issue date: 07 July 1986 (Syngenta File No. CGA169374/0050).</p> <p>2. Tack T. (1995). The determination of Difenconazole (CGA 169374) residues in soil after successive applications of A7402G 250EC containing 250 g ai CGA 169374 applied as a foliar application to winter wheat and bare soil for three years. Ciba-Geigy Ltd., Basel, Switzerland. Syngenta Unpublished Report No. CSTR 01:11. Issue date: October 1995 (Syngenta File No. CGA169374/1205).</p>
Method:	REM 7/86 (modified) , pre-registration method: Homogenized plant material is extracted with acetonitrile. An aliquot portion is evaporated to dryness. The residue is re-dissolved in acetonitrile and cleaned up by washing with n-hexane. The remaining acetonitrile phase is evaporated to dryness and the residue re-dissolved in n-hexane for further cleanup on a silica cartridge. After elution from the tube, the analyte is partitioned from aqueous methanol into hexane/ether (4 vol. + 1 vol.). Determination is by gas chromatography with electron capture detection (ECD).
GLP:	1. No; 2. yes.
Validation Data:	
Specificity:	GC-ECD is a specific quantification technique and allows the separation of the analyte from interferences. Residues of difenoconazole in the control samples were below LOQ.
Linearity:	No information given in report.
Accuracy:	The accuracy, as determined by mean recoveries at fortification levels from 0.05 – 0.5 mg/kg ranged from 78% to 95% (overall mean: 87%; N=22) with individual recoveries ranging from 71 – 111% (see summary table below).
Precision (Repeatability):	Precision under repeatability conditions was within the requirements of EU-guidance (RSD ≤ 20%).
LOQ:	0.05 mg/kg for soil (at this fortification level, the corresponding mean recovery was between 70% and 110% and RSD was ≤ 20%). <u>Remark: In the field trial the LOQ was given as 0.02 mg/kg, since at that time there was no explicit link between LOQ and the lowest fortification level.</u>
LOD:	nd

RMS comments: Method REM 7/86 is not considered a fully validated quantitative method for the determination of residues of difenoconazole in soil. Validation/data does not fulfil the criteria in SANCO/3029/99 rev.4, 11/07/00: Linearity/calibration is not reported (also wrong report of LOQ in the field trial).

Reference:	<p>1. Kühne-Thu H. (1997a). Determination of metabolite CGA 205375 by HPLC-UV – Soil. Novartis Crop Protection AG, Basel, Switzerland. Unpublished Report No. REM 147.04 Issue date: March 1997 (Syngenta File No. CGA169374/1387).</p> <p>2. Kühne-Thu H. (1997b). Validation of Method REM 147.04 – Validation by Analysis of Fortified Specimens and Determination of Recoveries; Extractability Test. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. 143/96 Issue date: February 1997 (Syngenta File No. CGA169374/1386).</p>
Method:	REM 147.04 , pre-registration method, determination of CGA 205375 (metabolite of

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difenoconazole) residues in soil: Homogenized soil samples are extracted with methanol/aqueous ammonium hydroxide solution (8 vol. + 2 vol.) by heating under reflux for two hours. An aliquot of the clear extract is diluted with water and sodium chloride solution. The analyte is partitioned into tertiary -butyl methyl ether (MTBE). The organic phase is evaporated to dryness and the residue re-dissolved in diethyl ether. After dilution with n-hexane the solution is loaded onto a pre-conditioned phenyl-coated silica column. After washing the column with hexane/diethyl ether rinses, the analyte is eluted with methanol. After evaporation, the residue is re-dissolved in acetonitrile and diluted with water. Final determination is performed on a two-column HPLC switching system with UV detection at 233 nm.

GLP: 1. No; 2. Yes.

Validation Data:

Specificity: The two-column switching reversed phase HPLC system with UV detection is specific and allows the separation of the analyte from interferences. Residues of CGA 205375 in the control samples were below LOQ.

Linearity: Linearity of detector response for CGA 205375 was demonstrated over the concentration range 0.01 µg/ml – 0.10 µg/ml (equivalent to the range of injected analyte amount of 1.0 ng – 10 ng with 100 µL injection volume; $r^2 = 0.9982$).

Accuracy: The accuracy, as determined by mean recoveries at fortification levels from 0.02 – 0.2 mg/kg ranged from 97% to 103% (overall mean: 100%; N=18) with individual recoveries ranging from 96 – 110% (see summary table below).

Precision (Repeatability): Precision under repeatability conditions was within the requirements of EU-guidance ($RSD \leq 20\%$).

LOQ: 0.02 mg/kg for soil (at this fortification level, the corresponding mean recovery was between 70% and 110% and RSD was $\leq 20\%$).

LOD: nd

RMS comments: Method REM 147.04 is a valid and accurate method for the determination of residues of CGA 205375 in soil. Validation data complies with the criteria in SANCO/3029/99 rev.4, 11/07/00.

Reference:

- 1. Formica G. (1992a).** Determination of free 1,2,4-triazole by high performance liquid chromatography – Propiconazole (CGA 64250) – Soil. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. REM 130.04 Issue date: June 1992 (Syngenta File No. CGA64250/2024).
- 2. Sack S. (1994).** Validation statements for methods REM 3/86, REM 130.02, REM 130.04 and REM 130.06. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished document Issue date: April 1994 (Syngenta File No. CGA64250/2345).
- 3. Kühne-Thu H. (2000).** Long term study on fate and behaviour of Difenoconazole (CGA 169374) in soil in Switzerland. Novartis Crop Protection AG, Basel, Switzerland. Unpublished Report No. 2031/89-98 Issue date: April 2000 (Syngenta File No. CGA169374/0652).

Method:

REM 130.04, pre-registration method, determination of 1,2,4-triazole (free triazole,

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metabolite of difenoconazole) residues in soil: Homogenized samples are extracted with water by shaking for 30 minutes. After centrifugation, an aliquot is submitted to derivatization of the free triazole with 2,4-dinitrofluorobenzene. After the chemical conversion into CGA 213291 (the derivative) the solution is loaded onto a pre-conditioned octadecyl-coated (C18) silica column. After washing the column with water, the columns are pre-eluted with water/acetonitrile (8 vol. + 2 vol.). The derivative is eluted with water/acetonitrile (6 vol. + 4 vol.). The eluate is evaporated to dryness. After re-dissolving the residue in diisopropylether/acetonitrile (9 vol. + 1 vol.), if necessary for clean-up the solution is loaded on a pre-conditioned silica gel column. The final eluate is evaporated to dryness. The residue is re-dissolved in tert.-butylmethylether (MTBE). The final determination is performed on a two-column HPLC switching system with UV detection at 270 nm.

GLP: 1. Yes; 2. Yes; 3. Yes.

Validation Data:

Specificity: Column switched HPLC-UV is a specific quantification technique and allows the separation of the analyte from interferences. Residues in the control samples were below LOQ. 1,2,4-triazole is not only a metabolite of difenoconazole but also of several other active ingredients.

Linearity: Linearity of detector response for CGA 213291 (derivative; HPLC-UV) was demonstrated over the concentration range 0.01 µg/ml – 0.2 µg/ml (equivalent to the range of injected analyte amount of 0.6 ng – 12 ng with 60 µL injection volume; $r^2 = 0.9982$).

Accuracy: The accuracy, as determined by mean recoveries at fortification levels from 0.01 – 0.2 mg/kg ranged from 65% to 77% (overall mean: 73%; N=16) with individual recoveries ranging from 58 – 91% (see summary table below).

Precision (Repeatability): Precision under repeatability conditions was within the requirements of EU-guidance ($RSD \leq 20\%$).

LOQ: 0.01 mg/kg for soil (at this fortification level, the corresponding mean recovery (66%) was only slightly below 70% and RSD was $\leq 20\%$).

LOD: nd

RMS comments: Method REM 130.04 is considered a valid and accurate method for the determination of 1,2,4-triazole residues in soil. Validation/data complies mostly with the criteria in SANCO/3029/99 rev.4, 11/07/00, although some mean recoveries are slightly below 70%.

Reference:

1. Formica G. (1992b), CGA 71818 (Penconazole) – Determination of total residues of CGA 71818 as 1,2,4-triazole by high performance liquid chromatography – Soil, fruits.

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	<p>Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. REM 107.06 Issue date: April 1992(Syngenta File No. CGA71818/0942).</p> <p>2. Kühne-Thu H. (2000). Long term study on fate and behaviour of Difenconazole (CGA 169374) in soil in Switzerland. Novartis Crop Protection AG, Basel, Switzerland. Unpublished Report No. 2031/89-98 Issue date: April 2000(Syngenta File No. CGA169374/0652)</p>
Method:	<p>REM 107.6, pre-registration method, determination of the combined residues (total triazole residues) of triazole-fungicides and their metabolites, which contain the 1,2,4-triazole common moiety in soil: A representative soil sample is extracted by refluxing in methanol/concentrated aqueous ammonium hydroxide (8 vol. + 2 vol.) for one hour. The mixture is cooled and filtered. An aliquot of the extract is concentrated and submitted to oxidation by refluxing with alkaline potassium permanganate. The excess of permanganate is reduced to manganese dioxide with ethanol. The mixture is filtered and the aqueous phase is adjusted to about pH 9. An aliquot is concentrated and 1,2,4-triazole is derivatized to CGA 213291 with 2,4-dinitrofluorobenzene. The derivative is cleaned up by passage first through a partition column and thereafter through an adsorption column prior to quantification by liquid chromatography (HPLC) using column switching techniques and UV-detection at 270 nm.</p>
GLP:	1. No; 2. Yes.
Validation Data:	
Specificity:	This method is a common moiety method and determines all compounds, which can be converted to 1,2,4-triazole under the used conditions. Residues in the control samples were below LOQ.
Linearity:	Linearity of detector response for CGA 213291 (derivative; HPLC-UV) was demonstrated over the concentration range 2.5 ng/ml – 40 ng/ml (equivalent to the range of injected analyte amount of 0.15 ng – 2.4 ng with 60 µL injection volume; $r^2 = 0.9901$).
Accuracy:	The accuracy, as determined by mean recoveries at fortification levels from 0.05 – 0.5 mg/kg ranged from 74% to 88% (overall mean: 81%; N=12) with individual recoveries ranging from 53 – 101% (see summary table below).
Precision (Repeatability):	Precision under repeatability conditions was within the requirements of EU-guidance ($RSD \leq 20\%$).
LOQ:	0.05 mg/kg for soil (at this fortification level, the corresponding mean recovery was between 70% and 110% and RSD was $\leq 20\%$). LOQ is expressed in parent equivalents.
LOD:	nd

RMS comments: Method REM 107.06 is a valid and accurate method for the determination of total difenconazole residues (1,2,4-triazole common moiety) in soil. Validation/data complies with the criteria in SANCO/3029/99 rev.4, 11/07/00.

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Table 5.3.1-3: Summary of method validation data (difenoconazole and metabolites in soil)

Reference	Matrix	Fortification Level(mg/kg)	Recovery (%)		SD (%)	RSD (%)	N
			Mean	Range			
RAM 421/01 Tummon (2004a) (LC-MS/MS)	Sandy loam	0.01	97	91 – 104	-	5	5
		0.1	92	82 – 100	-	9	5
		Overall	95	82 – 104	-	7	10
RAM 421/01 Tummon (2004a) (LC-MS/MS)	Silty clay loam	0.01	88	81 – 95	-	5	5
		0.1	84	75 – 95	-	9	5
		Overall	86	75 – 95	-	7	10
AG-501 Williams (1986) (GC-NPD)	Silty clay loam	0.05	100	89 – 111	15.6	15.6	2
		0.1, 0.5 & 1.0	104	99 – 109	5.0	4.8	3
		Overall	103	89 – 111	8.9	8.7	5
AG-501 Williams (1986) (GC-NPD)	Everglades peat	0.05	117	112 – 121	6.4	5.5	2
		0.1, 0.5 & 1.0	116	105 – 134	15.5	13.3	3
		Overall	116	105 – 134	11.4	9.8	5
AG-501 Williams (1986) (GC-NPD)	Silt loam	0.05	98	93 – 103	7.1	7.2	2
		0.1, 0.5 & 1.0	107	102 – 115	7.2	6.8	3
		Overall	103	93 – 115	7.8	7.6	5
AG-501 Williams (1986) (GC-NPD)	Sand	0.05	87	82 – 92	7.1	8.1	2
		0.1, 0.5 & 1.0	99	95 – 106	5.9	5.9	3
		Overall	94	82 – 106	8.7	9.2	5
AG-501 Williams (1986) (GC-NPD)	Clay	0.05	106	100 – 111	7.8	7.4	2
		0.1, 0.5 & 1.0	103	101 – 107	3.5	3.4	3
		Overall	104	100 – 111	4.8	4.6	5
AG-501 Williams (1986) (GC-NPD)	Sandy loam	0.05	105	99 – 110	7.8	7.4	2
		0.1, 0.5 & 1.0	108	106 – 112	3.5	3.2	3
		Overall	107	99 – 112	5.0	4.7	5
AG-501 Williams (1986) (GC-NPD)	Overall soil	0.05	102	82 – 121	11.5	11.3	12
		0.1, 0.5 & 1.0	106	95 – 134	8.6	8.1	18
		Overall	105	99 – 110	7.8	7.4	30
AG-501 mod. (from several trials) (GC-ECD)	Overall soil	0.04	112	101 – 119	7.1	6.3	5
		0.2	109	107 – 113	3.2	2.9	3
		Overall	111	101 – 119	5.8	5.2	8
AG-514 mod. (from several trials) (GC-ECD)	Overall soil	0.04	106	87 – 119	11.0	10.4	18
		0.2	105	93 – 122	7.0	6.7	16
		Overall	105	87 – 122	9.2	8.7	34

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Reference	Matrix	Fortification Level(mg/kg)	Recovery (%)		SD (%)	RSD (%)	N
			Mean	Range			
AG-575A mod. (from several trials) (GC-ECD)	Sandy loam & loam	0.02	99	85 – 115	11.1	11.2	6
		0.04	95	90 – 101	5.5	5.8	3
		0.2	104	99 – 110	4.0	3.8	7
		(0.04 & 0.2)	102	90 – 110	6.9	5.9	10
		Overall	101	85 – 115	8.0	7.9	16
M-501/514 (from several trials) (GC-NPD, GC-ECD)		0.05	92	83 – 114	11.6	12.5	6
		0.1 & 0.5	97	70 – 130	18.0	18.5	11
		1.0, 1.5 & 5	93	81 – 112	8.9	9.6	10
		Overall	94	70 – 130	13.5	14.3	27
REM 7/86 mod. Tack T. (1995)	Overall	0.05	85	76 – 99	8.8	10.4	8
		0.1	95	75 – 111	17.5	18.5	8
		0.5	78	71 – 87	6.1	7.8	6
		Overall	87	71 – 111	13.6	15.7	22
REM 147.04 Val. report 143/96 Kühne-Thu (1997) <u>CGA 205375</u>	Loam	0.02	98	96 – 102	3.2	3.3	3
		0.20	107	106 – 110	2.3	2.2	3
	Sandy loam	0.02	98	97 – 100	1.5	2.3	3
		0.20	99	96 – 100	1.6	2.3	3
	Sand	0.02	97	96 – 99	1.7	1.8	3
		0.20	102	99 – 107	4.2	4.1	3
	Overall soil	0.02	98	96 – 102	2.1	2.1	9
		0.2	103	96 – 110	4.6	4.5	9
		Overall	100	96 – 110	4.3	4.3	18
REM 130.04 <u>1,2,4-triazole</u> Formica (1992a) (HPLC-UV)	Overall soil	0.02	74	63 – 86	11.9	16.1	4
		0.2	74	68 – 79	4.5	6.1	4
REM 130.04 Sack (1994) (HPLC-UV)	Overall soil	0.02	77	63 – 107	14.2	18.4	9
		0.2	75	64 – 91	9.0	12.0	9
REM 130.04 (from several trials) (HPLC-UV)	Overall soil	0.01	66	63 – 69	3.1	4.7	3
		0.1	65	58 – 78	11.3	17.3	3
REM 130.04 Overall (HPLC-UV)	Overall soil	0.01	66	63 – 69	3.1	4.7	3
		0.02	76	63 – 107	13.2	17.2	13
		0.1	73	58 – 91	8.9	12.2	16
		Overall	74	58 – 107	10.7	14.6	32
REM 107.06 <u>mod.total residues</u> Kühne-Thu (2000) (HPLC-UV)	Overall soil	0.05	88	62 – 101	13.5	15.5	6
		0.5	74	53 – 82	10.9	14.6	6
		Overall	81	53 – 101	13.6	16.8	12

B.5.3.2 Analytical method for the determination of residues in surface water and drinking water (potable water)**Reference:**

- 1. Tribolet R. (1999a).** Determination of parent compound by gas chromatography – Difenoconazole (CGA 169374) – Water. Novartis Crop Protection AG, Basel, Switzerland. Unpublished Report No. REM 147.05 Issue date: January 1999 (Syngenta File No. CGA169374/1783).
- 2. Tribolet R. (1999b).** Validation of method REM 147.05 by analysis of fortified water specimens for difenoconazole (CGA 169374) and evaluation of recoveries. Novartis Crop Protection AG, Basel, Switzerland. Unpublished Report No. 226/98 Issue date: January 1999 (Syngenta File No. CGA169374/1782).

Method:

REM 147.05, proposed as a monitoring method for the determination of difenoconazole residues in water:

A small amount of ethanol is added to a water sample that is passed through a pre-conditioned phenyl bonded solid phase extraction column (SPE). After washing the SPE column with water, difenoconazole is eluted with ethanol. The eluate is evaporated to dryness and the residue re-dissolved in ethyl acetate, containing small amounts of polyethylene glycol (0.025% w/v). Difenoconazole is determined by gas chromatography (GC) using electron capture detection (ECD).

Confirmatory techniques:

Approach a) Determination with HPLC can be used as confirmatory technique: An aliquot of the final solution is evaporated to dryness. The residue is dissolved in acetonitrile/water/methanol (75 vol. + 25 vol.) instead of toluene. Final determination is performed with a two column switching reversed phase liquid chromatography system (HPLC) with UV detection. This approach is described in the method.

Approach b) After evaporating the eluate to dryness the final determination of difenoconazole can be made using the LC-MS/MS detection of method RAM 421/01, see above, analysis of soil, (sample taken up in acetonitrile/water solution (30:70, v/v) prior to injection on to the column)

GLP:

No.

Validation Data:

Validated for both surface and drinking (potable) water.

Specificity:

GC-ECD is a specific quantification technique and allows the separation of the analyte from interferences. Residues of difenoconazole in the control samples were below LOQ. Confirmation: see method above.

Linearity:

Linearity of detector response for difenoconazole (GC-ECD) was demonstrated over the concentration range (n=5) 0.004 µg/ml – 0.08 µg/ml (equivalent to the range of injected analyte amount of 0.02 ng – 0.4 ng with 5 µL injection volume); $r^2 = 0.9997$.

Accuracy:

The accuracy, as determined by mean recoveries at fortification levels from

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0.05 – 1.0 µg/l ranged from 73% to 96% (overall mean: 85%; N=20) with individual recoveries ranging from 68 – 97%; see table below.

Precision (Repeatability): Precision under repeatability conditions was acceptable (RSD ≤ 20%).

LOQ: 0.05 µg/l for potable water and 0.1 µg/l for surface water (at these fortification levels, the corresponding mean recovery was between 70% and 110% and RSD was ≤ 20%).

The LOQ for surface water is below the lowest chronic NOEC (5.6 µg/l) observed in studies on toxicity to aquatic organisms (*daphnia*) and is therefore in compliance with the criterion in SANCO/825/00, rev. 7.

LOD: nd.

Results:

Table 5.3.2-1: Recovery of Difenoconazole from drinking (potable) water

substrate	fortification level	control [µg/mL]	recoveries [%] ¹⁾	\bar{X} [%]	s_{abs} [%]	s_{rel} [%]	N
potable water	0.05 µg/L	<0.05	93, 91, 86, 92, 91 (1)	91	2.7	3.0	5
	0.5 µg/L	<0.05	96, 97, 96, 96, 93 (1)	96	1.5	1.6	5
surface water (Rhine)	0.1 µg/L	<0.1	73, 68, 73, 74, 76 (2)	73	2.9	4.1	5
	1.0 µg/L	<0.1	78, 79, 81, 79, 78 (2)	79	1.2	1.6	5

1) numbers in parenthesis: reference number for further analytical details (cf. section 10.3)

RMS comments:

Method REM 147.05 is a valid and accurate method for the determination of difenoconazole residues in potable and surface water (validation/data complies with the criteria in SANCO/825/00 rev. 7, 17/03/2004). It is concluded that this method can be used in normal routine analysis and for monitoring purposes.

Reference: **Tribolet R. (1990).** Determination of residues of parent compound by gas liquid chromatography (GLC) – CGA 169374 – Potable water. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. REM 147.01 Issue date: May 1990(Syngenta File No. CGA169374/0055).

Method: **REM 147.01**, pre-registration metod: A small amount of ethanol is added to a water sample that is passed through a pre-conditioned phenyl bonded solid phase extraction column (SPE). After washing the SPE column with water, difenoconazole is eluted with ethanol. The eluate is evaporated to dryness and the residue re-dissolved in toluene. Difenoconazole is determined by gas chromatography (GC) using electron capture detection (ECD).

GLP: No

Validation Data:

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Specificity:	GC-ECD is a specific quantification technique and allows the separation of the analyte from interferences. Residues of difenoconazole in the control samples were below LOQ. HPLC-UV can be used for confirmation.
Linearity:	Calibration with external standards in concentration ranges 0.0025 µg/ml – 0.06 µg/ml (equivalent to the injected mass range 0.0125 ng – 0.3 ng with 5 µL injection volume). Evaluation is by linear regression; sd=8.5%
Accuracy:	The accuracy, as determined by mean recoveries at fortification levels from 0.1 – 1.0 µg/l ranged from 90% to 96% (overall mean: 93%; N=20) with individual recoveries ranging from 83 – 105%, see summary table below.
Precision (Repeatability):	Precision under repeatability conditions was within the requirements of EU-guidance (relative standard deviation (RSD) ≤ 20%), see summary table below
LOQ:	0.1 µg/l for HPLC-grade water and potable water (at this fortification level, the corresponding mean recovery was between 70% and 110% and RSD was ≤ 20%).
LOD:	nd

RMS comments: Method REM 147.01 is a valid and accurate method for the determination of difenoconazole residues in potable water. Validation/data complies with the criteria in SANCO/3029/99 rev.4, 11/07/00.

Table 5.3.2-2: Summary of validation data for REM 147.01 and REM 147.05 (difenoconazole in drinking/potable and surface water).

Reference	Matrix	Fortification Level (µg/l)	Recovery (%)		SD (%)	RSD (%)	N
			Mean	Range			
REM 147.01 Tribolet (1990) (GC-ECD)	HPLC-grade water	0.1	96	83 – 105	9.3	9.7	4
		1.0	92	87 – 97	4.8	5.2	4
		Overall	94	83 – 105	7.2	7.7	8
REM 147.01 Tribolet (1990) (GC-ECD)	Potable water	0.1	90	84 – 97	5.5	6.0	6
		1.0	95	87 – 101	5.0	5.3	6
		Overall	93	84 – 101	5.7	6.1	12
All data REM 147.01 (GC-ECD)	Overall water	Overall	93	83 – 105	6.1	6.6	20
REM 147.01 Tribolet (1990) HPLC-UV (Confirm. technique)	Potable water	0.1	92	83 – 100	7.9	8.6	4
		1.0	90	87 – 93	2.8	3.1	4
		Overall	91	83 – 100	5.6	6.2	8
REM 147.05 Val. report 226/98 Tribolet (1999b) (GC-ECD)	Potable water	0.05	91	86 – 93	2.7	3.0	5
		0.50	96	93 – 97	1.5	1.6	5
		Overall	93	86 – 97	3.3	3.6	10

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Reference	Matrix	Fortification Level (µg/l)	Recovery (%)		SD (%)	RSD (%)	N
			Mean	Range			
REM 147.05Val. report 226/98 Tribolet (1999b) (GC-ECD)	Surface water	0.1	73	68 – 76	2.9	4.1	5
		1.0	79	78 – 81	1.2	1.6	5
		Overall	76	68 – 81	3.9	5.1	10
All data REM 147.05 (GC-ECD)	Overall water	Overall	85	68 – 97	9.5	11.2	20
REM 147.05 Tribolet (1999a) HPLC-UV (Confirm. technique)	Surface water	0.1	85	78 – 91	9.2	10.9	2
		1.0	62	61 – 62	0.7	1.1	2
		Overall	73	61 – 91	14.3	19.6	4

B.5.3.4 Analytical method for the determination of residues in air

Reference: **Tummon O.J. (2004b).** Difenoconazole: Validation of an analytical method for the determination of residues in air. Syngenta, Jealott's Hill International Research Centre, Bracknell, UK. Unpublished Report No. RJ3495B. Issue date: 21 April 2004, Syngenta File No. CGA169374/2500.

Method: **RAM 422/01**, proposed as a monitoring method for the determination of difenoconazole residues in air:

Method: Air is drawn through a sampling tube containing two layers of XAD-2 adsorbent at a rate of 0.5 L/min for a period of up to six hours, using a pre-calibrated motorized pump. After this time period the XAD-2 adsorbent is removed from the tube and the residue of difenoconazole is desorbed by ultrasonication in acetonitrile. An aliquot of the acetonitrile is then diluted with ultra pure water. Final determination is by high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS).

The limit of quantification (LOQ) is 0.99 ng/l, equivalent to 0.178 µg adsorbed on the XAD-2 sorbent.

GLP: Yes.

Validation Data:

Specificity: LC-MS/MS is a highly specific quantification technique and allows the separation of the analyte from interferences. Residues of difenoconazole in the control samples were less than 30% of the LOQ.

Linearity: Linearity of detector response for difenoconazole was demonstrated over the concentration range (n=5) 0.0005 µg/ml – 0.25 µg/ml (equivalent to the range of injected analyte amount of 5 pg – 2.5 ng with a 10 µL injection volume; $r^2 = 1.0$).

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Accuracy:	The accuracy, as determined by mean procedural recoveries were between 70 and 110% at each fortification level; see table below.
Precision (Repeatability):	Precision under repeatability conditions was within the requirements of EU-guidance (relative standard deviation (RSD) $\leq 20\%$); see table below.
LOQ:	The LOQ was 0.99 ng/l for difenoconazole in air, which is equal to <u>0.99 $\mu\text{g}/\text{m}^3$</u> The criterion in SANCO/825/00, rev. 7 for the LOQ of the analytical method is that it should be equal or lower than: $C = \frac{AOEL \cdot 0.1 \cdot 60}{20} [\text{mg} / \text{m}^3 \text{air}]$ <p>The analytical method for the determination of residues of difenoconazole in air complies with this criterion since the LOQ is lower than C, which using an AOEL of 0.2 mg/kg bw/day, is equal to 0.06 mg/m³air.</p>
LOD:	nd.

Results:**Table 5.3.4-1: Recovery of Difenoconazole from air using RAM 422/01**

Conditions	Fortification Level (μg)	Recovery (%)	Mean (%)	RSD (%)	Range
35°C at 80 % Relative humidity 6 hr monitoring	control	ND, ND**			
	0.99*	83, 90, 73, 75, 66	77	12	66-90
	9.9	87, 88, 91, 83, 90	88	4	83-91
	Overall		83	9	66-91

*Limit of quantification, defined by the lowest validated fortification level

ND** No residues detected in the control samples at or above LOQ

RMS comments:

Method RAM 422/01 is suitable for monitoring difenoconazole residues in air (validation/data complies with SANCO/825/00 rev. 7, 17/03/2004).

Note: Data from tests using air particles is not reported or discussed, but the notifier has argued convincingly in an additional document that all air particles are trapped at the adsorbent.

Reference:

1. Tribolet R. (1992). Sampling of air and determination of residues of parent compound by gas chromatography – Difenoconazole (CGA 169374) – Air. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. REM 147.02 Issue date: December 1992(Syngenta File No. CGA169374/0722).

2. Tribolet R. (1996). Validation of method REM 147.02 in air – Validation by analysis of fortified specimens and determination of recoveries. Ciba-Geigy Ltd., Basel, Switzerland. Unpublished Report No. 102/96 Issue date: February 1996(Syngenta File N° CGA169374/1192).

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Method: **REM 147.02**, proposed as a monitoring method: A defined volume of air is sucked through a sorbent tube using an air sampler pump. The different layers of the tube are separated and difenoconazole is extracted with methanol using an ultrasonic bath. The methanol is evaporated and the residue is re-dissolved in toluene. Difenoconazole is determined by gas chromatography using an ECD detector. The limit of quantification is 2 µg/m³.

GLP: 1. No; 2. Yes.

Validation Data:

Specificity: GC-ECD is a specific quantification technique and allows the separation of the analyte from interferences. Residues of difenoconazole in the control samples were below LOQ. RAM 422/01 can be used for confirmation.

Linearity: Linearity of detector response for difenoconazole was demonstrated over the concentration range 0.04 µg/ml – 0.5 µg/ml (equivalent to the range of injected analyte amount of 0.08 ng – 1.0 ng with 2 µL injection volume; $r^2 = 0.9924$).

Accuracy: The accuracy, as determined by mean recoveries at fortification levels from 1 – 50 µg/m³ ranged from 80% to 86% (overall mean: 84%) with individual recoveries ranging from 77 – 93%.

Precision (Repeatability): Precision under repeatability conditions was within the requirements of EU-guidance (relative standard deviation (RSD) ≤ 20%).

LOQ: 1 µg/m³ (at this fortification level, the corresponding mean recovery was between 70% and 110% and RSD was ≤ 20%).

The criterion in SANCO/825/00, rev. 7 for the LOQ of the analytical method is that it should be equal or lower than:

$$C = \frac{AOEL \cdot 0.1 \cdot 60}{20} [mg / m^3 air]$$

The analytical method for the determination of residues of difenoconazole in air complies with this criterion since the LOQ is lower than C, which using an AOEL of 0.2 mg/kg bw/day, is equal to 0.06 mg/m³ air.

LOD: nd

Table 5.3.4-2: Summary validation data for RAM 422/01 and REM 147.02 (difenoconazole in air).

Reference	Matrix	Fortification Level	Recovery (%)		SD (%)	RSD (%)	N
			Mean	Range			
RAM 422/01 Tummon (2004b) LC-MS/MS	Air (~33°C, ~73% relative humidity)	0.99 ng/l	77	66 – 90	-	12	5
		9.9 ng/l	88	83 – 91	-	4	5
		Overall	83	66 – 91	-	9	10
RAM 422/01 Tummon (2004b) LC-MS/MS	Air (20°C, ambient humidity)	10 ng/l	91	88 – 95	-	3	5
		20000 ng/l	85	75 – 97	-	10	5
		Overall	88	75 – 97	-	7	10

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REM 147.02 Val. Report 114/92 included in Tribolet (1992) GC-ECD	Air (22°C, 49% rel. hum. or 12°C, 86% rel. hum.)	2 mg/m ³ 4 mg/m ³ 20 mg/m ³ Overall	81 80 83 81	77 – 84 79 – 81 81 – 85 77 – 85	4.9 1.4 2.8 3.0	6.1 1.8 3.4 3.7	2 2 2 6
REM 147.02 Val. Report 102/96 Tribolet (1996) GC-ECD	Air (35°C, 80% rel. hum.)	1 mg/m ³ 50 mg/m ³ Overall	86 85 85	77 – 90 82 – 93 77 – 93	4.5 3.6 3.9	5.2 4.2 4.6	8 8 16
Both val. reports	Overall air	Overall	84	77 – 93	4.1	4.8	22

RMS comments: Method REM 147.02 is a valid and accurate method for the determination of difenoconazole residues in air. It is concluded that this method can be used in normal routine analysis and for monitoring purposes. Validation/data complies with SANCO/825/00 rev. 7, 17/03/2004.

B.5.4 Analytical methods (residue) for body fluids and tissues (Annex IIA 4.2.5; Annex IIIA 5.2)

Not relevant for this pesticide (difenoconazole is not toxic or highly toxic.).

B.5.5 Evaluation and assessment

Although the two methods AG-514 (analysis of difenoconazole in tomatoes and potato tubers), and AG-537/537A (analysis of difenoconazole in carrot) were not considered fully validated methods taken separately they are never the less considered validated and acceptable since they together with AG-575A form a cluster of methods that are almost similar and could be viewed as one method. With that condition the validation basis is fulfilling requirements. AG-575A itself was considered acceptable in the first place.

AG-544A is not considered a fully validated quantitative method for the analysis of difenoconazole in milk, kidney, liver and eggs because sample sets are incomplete. Validation/data are acceptable for muscle and fat, though. However, according to the notifier this method has not been used in any study supporting the application (and it is not a monitoring method). Validation/data do also support the AG-544A modified version (main purpose with these data according to the notifier). The LOQ of AG-544A modified is slightly uncertain, because of incomplete dataset at the LOQ level. According to the notifier the feeding study that uses data based on this method will soon be superseded by a new study that uses data based on another method (the acceptable monitoring method REM 147.07).

REM 7/86 (analysis of difenoconazole in soil) is not considered a fully validated quantitative method because there is no data on linearity.

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All other analytical methods/validations are acceptable for their purpose, although there are some data of minor importance that not fully complies with the criteria in, respectively, SANCO/3030/99 rev.4, 11/07/00, SANCO/825/00 rev. 7, 17/03/2004 or SANCO/3029/99 rev.4, 11/07/00.

B.5.5.1 Analytical methods for technical active substance and formulation analysis

Table B.5.5.1: Summary of analytical methods for technical active substance and formulation analysis

Matrix	Substance	Detection technique	LOQ	Reference
Technical grade	Difenoconazole	GC-FID	-	1. Kaser, W., 2000a. 2. Kaeser, W., 2000b
Technical grade	Impurities (see Annex C)	Confidential (see Annex C)	-	1. Kaeser, W., 2002b CONFIDENTIAL INFORMATION. 2. Stampf, Ph., 2002, CONFIDENTIAL INFORMATION
Formulation (Dividend)	Difenoconazole	RP HPLC-UV	-	1. Kaeser, W., 1999 2. Kaeser, W., 1999a
Formulation (Score)	Difenoconazole	GC-FID	-	1. Kaeser, W., 1992 2. Kaeser, W., 1994 3. Krips, W., 1998

B.5.5.2 Analytical methods for determination of residues in plant and animal products, soil, water, air and body fluids and tissues

Table B.5.5.1: Summary of analytical methods for determination of residues in food/feed of plant origin, soil, water and air

Matrix		Substance	Detection technique	LOQ	Reference
Crops	Apple	Difenoconazole	LC-MS/MS	0.01 mg/kg	1. Steinhauer S. 2004a 2. Schulz H. 2004
	Lettuce				
	Wheat (grain)				
	Oil Seed Rape				
Crops	Tomatoes	Difenoconazole	GC-NPD	0.05 mg/kg	Williams W.L., Shoffner K.P. 1987
	Potatoes				
Crops	Wheat raw agric.	Difenoconazole	GC-NPD	0.05 mg/kg	1. Williams W.L. 1988 2. Whetzel J.E. 1990
Crops	Wheat raw agric.	Difenoconazole	GC-NPD	0.01 mg/kg	Ross J. 1991
	Apple/pear				
	Carrot				
Crops	Carrot	Difenoconazole	GC-ECD	0.04 mg/kg	Bussy L., Maffezzoni M. 1993
Animal	Bovine Liver	Difenoconazole, CGA 205375 (metabolite)	LC-MS/MS	0.01 mg/kg	1. Crook S.J. 2004 2. Ryan J. 2004b 3. Benazeraf L. 2004
	Bovine Kidney				
	Bovine Muscle				
	Bovine Fat				
	Bovine Milk				
	Hen Eggs				
Animal	Milk	Difenoconazole	GC-NPD	0.01 mg/kg (milk) 0.05 mg/kg	Wurz R.E.M. 1994
	Muscle				
	Fat				
	Liver				
	Kidney				
	Eggs				

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Matrix		Substance	Detection technique	LOQ	Reference
Animal	Milk	Difenoconazole, CGA 205375 (metabolite)	LC-MS/MS	0.01 mg/kg 10 µg/l (blood) 5 µg/l (milk)	Tribolet, R. 2000
	Muscle				
	Fat				
	Liver				
	Kidney				
	Blood				
Soil		Difenoconazole, CGA 205375 (metabolite)	LC-MS/MS	0.01 mg/kg	Tummon O.K. 2004a
Soil	Silty clay loam	Difenoconazole	GC-NPD GC-ECD	0.04 - 0.05 mg/kg	1. Williams R.K. 1986 2. Kühne-Thu H. 1990a 3. Kühne-Thu H. 1990b
	Everglades peat				
	Silt loam				
	Sand				
	Clay				
	Sandy loam				
Soil	Overall soil	Difenoconazole	GC-ECD	0.04 mg/kg	1. Williams, R.K. Shoffner, K.P. 1987 2. Kühne-Thu H. 2000 3. Kühne-Thu H. 1990c 4. Kühne-Thu H. 1990d 5. Kühne-Thu H. 1991a 6. Kühne-Thu H. 1991b 7. Kühne-Thu H. 1990b 8. Kühne-Thu H. 1990a
Soil	Sandy loam & loam	Difenoconazole	GC-ECD	0.02 mg/kg	1. Ross, J. 1991 2. Kühne-Thu H. 2000 3. Kühne-Thu H. 1992 4. Ross, J. 1991
Soil	Overall soil	Difenoconazole	GC-ECD	0.05 mg/kg	1. Kühne-Thu H. 1986 2. Tack T. 1995
Soil	Loam	CGA 205375 (metabolite)	HPLC-UV	0.02 mg/kg	1. Kühne-Thu H. 1997a 2. Kühne-Thu H. 1997b
	Sandy loam				
	Sand				
	Over all soil				
Soil	Overall soil	2,4-triazole (free metabolite)	HPLC-UV	0.01 mg/kg	1. Formica G. 1992a 2. Sack S. 1994 3. Kühne-Thu H. 2000
Soil	Overall soil	2,4-triazole (metabolite; common moiety)	HPLC-UV	0.05 mg/kg	1. Formica G. 1992a 2. Sack S. 1994 3. Kühne-Thu H. 2000
Water	Surface water	Difenoconazole	GC-ECD	0.05-0.1 µg/l	1. Tribolet R. 1999a 2. Tribolet R. 1999b
	Drinking-water (potable)				
Water	HPLC-grade	Difenoconazole	GC-ECD	0.1 µg/l	Tribolet R. 1990
	Drinking-water (potable)				
Air	Air (ca 33°C, ca 73% relative humidity)	Difenoconazole	LC-MS/MS	0.99 ng/l	Tummon O.J. 2004b
	Air (20°C, ambient humidity)				
Air	Air (22°C, 49% relative humidity or 12°C, 86% relative humidity)	Difenoconazole	GC-ECD	1 ng/l	1. Tribolet R. 1992 2. Tribolet R. 1996
	Air (35°C, 80% relative humidity)				

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B.5.6 References relied on

Annex point / reference number	Author(s)	Year	Title Source (where different from company) Company, Report No GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N ⁱ	Owner ⁱⁱ
IIA 4.1.1/01	Käser, W.	2000a	Analytical method CGA 169374 tech. Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Müchwilen AG, Müchwilen, Switzerland, Report No AW- 128/3 Not GLP Not Published Syngenta File N° CGA169374/2064	Y	SYN
IIA 4.1.3/01	Käser, W.	2000b	Validation of analytical method AW-128/3 Syngenta Crop Protection AG, Basel, Switzerland Novartis Crop Protection Müchwilen AG, Müchwilen, Switzerland, Report No 81931 GLP Not Published Syngenta File N° CGA169374/2440	Y	SYN
IIA 4.2.1.1/01 IIA 4.2.1.2/01 IIA 4.2.2.1/03 IIA 4.2.2.2/04	Williams, R.K, Shoffner, K.P	1987	CGA 169374, Analytical method for the determination of CGA 169374 in tomatoes and potatoes by gas chromatography Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Corp., Greensboro, United States, Report No AG-514 GLP Not Published Syngenta File N° CGA169374/0052	N	SYN
IIA 4.2.1.1/02 IIA 4.2.1.2/02	Williams, W.L	1988	CGA 169374, Anal. Method for the determination of CGA 169374 in wheat raw agricultural commodities by gas chromatography Syngenta Crop Protection AG, Basel, Switzerland Ciba-Geigy Corp., Greensboro, United States, Report No AG-537 Not GLP Not Published Syngenta File N° CGA169374/0053	N	SYN

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Annex B.5: Analytical methods

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IIA 4.2.1.1/03 IIA 4.2.1.2/04 IIA 4.2.2.1/04 IIA 4.2.2.2/14	Ross, J.	1991	Anal. method for the determination of CGA 169374 in wheat raw agricultural commodities by gas chromatography with nitrogen/phosphorus detection Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Corp., Greensboro, United States, Report No AG-575A GLP Not Published Syngenta File N° CGA169374/0450	N	SYN
IIA 4.2.1.1/04	Bussy, L., Maffezzoni, M.	1993	Determination of CGA 169374 in vegetable matter, grapes and wine Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy SA, Rueil-Malmaison, France, Report No RES 10/93 Not GLP Not Published Syngenta File N° CGA169374/0900	N	SYN
IIA 4.2.1.1/05 IIA 4.2.1.2/06	Steinhauer, S.	2004a	Difenoconazole; Validation of the DFG Method S 19 (Extended Revision) for the Determination of residues of Difenoconazole in Apple, Oil Seed Rape, Wheat (Grain) and Lettuce Syngenta Crop Protection AG, Basel, Switzerland Dr. Specht & Partner Chem. Laboratorien GmbH, Hamburg, Germany, Report No SYN-0301V Az. G03-0012 GLP Not Published Syngenta File N° CGA169374/2428	Y	SYN
IIA 4.2.1.1/06 IIA 4.2.1.2/08	Wurz, R.E.M	1994	Analytical method for the determination of CGA 169374 residues in dairy and poultry tissue, eggs and milk by gas chromatography Syngenta Crop Protection AG, Basel, Switzerland Ciba-Geigy Corp., Greensboro, United States, Report No AG-544A Not GLP Not Published Syngenta File N° CGA169374/0933	N	SYN

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Annex B.5: Analytical methods

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IIA 4.2.1.1/07 IIA 4.2.1.2/10	Steinhauer, S.	2004b	Difenoconazole: Validation of the DFG Method S 19 (Extended Revision) for the Determination of Residues of Difenoconazole in Milk, Meat, Fat, Egg, Liver and Kidney Syngenta Crop Protection AG, Basel, Switzerland Dr. Specht & Partner Chem. Laboratorien GmbH, Hamburg, Germany, Report No SYN-0302V Az. G03-0024 GLP Not Published Syngenta File N° CGA169374/2443	Y	SYN
IIA 4.2.1.1/08 IIA 4.2.2.1/09 IIA 4.2.2.2/22	Crook, S.J.	2004	Residue Method for the Determination of Residues of Difenoconazole (CGA169374) and CGA 205375 in Animal Products. Final Determination by LC-MS/MS Syngenta Crop Protection AG, Basel, Switzerland Syngenta, Jealott's Hill, United Kingdom, Report No REM 147:07 Not GLP Not Published Syngenta File N° CGA205375/0021	Y	SYN
IIA 4.2.1.2/03	Whetzel, J.E.	1990	Method ruggedness trial for Ciba-Geigy Analytical Method no AG-537A for the determination of CGA 169374 in wheat raw agric. commodities by gas chromatography Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Corp., Greensboro, United States, Report No AG-537A GLP Not Published Syngenta File N° CGA169374/0619	N	SYN
IIA 4.2.1.2/05	Ryan, J.	2004a	Difenoconazole (CGA 169374): Summary of Validation Data for Analytical Method RES10/93 on Various Crops Syngenta Crop Protection AG, Basel, Switzerland Syngenta, Jealott's Hill, United Kingdom, Report No TMJ4940B Not GLP Not Published Syngenta File N° CGA169374/2421	Y	SYN

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IIA 4.2.1.2/07	Schulz, H.	2004	Independent Laboratory Validation of DFG Method S19 (Extended Revision) for the Determination of Residues of difenoconazole in/on plant matrices Syngenta Crop Protection AG, Basel, Switzerland Institut Fresenius, Taunusstein, Germany, Report No IF-04/00160619 GLP Not Published Syngenta File N° CGA169374/2507	Y	SYN
IIA 4.2.1.2/09	Tribolet, R.	2000	Residue of Difenoconazole (CGA 169374) and its Metabolite CGA 205375 in Milk, Blood, and Tissues (Muscle, Fat, Liver, Kidney) of Dairy Cattle Resulting From Feeding of Difenoconazole at Three Dose Levels Novartis Crop Protection AG, Basel, Switzerland, Report No 202/99 GLP Not Published Syngenta File N° CGA169374/2039	Y	SYN
IIA 4.2.1.2/11 IIA 4.2.2.2/21	Ryan, J.	2004b	Difenoconazole (CGA169374) and CGA205375: Validation of Residue Analytical Method REM 147.07 for the Determination of Residues in Animal Products Syngenta Crop Protection AG, Basel, Switzerland Syngenta, Jealott's Hill, United Kingdom, Report No RJ3478B GLP Not Published Syngenta File N° CGA205375/0020	Y	SYN
IIA 4.2.1.2/12	Benaseraf, L.	2004	Independent Laboratory Validation of Residue Method REM 147.07 for the Determination of Difenoconazole and CGA205375 in Animal Products Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergèze, France, Report No SYN/DIF/04031 GLP Not Published Syngenta File N° CGA169374/2535	Y	SYN

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IIA 4.2.2.1/01	Tummon, O. J.	2004a	Difenoconazole. Validation of an Analytical Method for the Determination of Residues of Difenoconazole and CGA205375 in Soil Syngenta Crop Protection AG, Basel, Switzerland Syngenta, Jealott's Hill, United Kingdom, Report No RJ3459B GLP Not Published Syngenta File N° CGA169374/2501	Y	SYN
IIA 4.2.2.1/02 IIA 4.2.2.2/01	Williams, R.K	1986	CGA 169374, Analytical method for the determination of CGA 169374 in soil by gas chromatography. Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Corp., Greensboro, United States, Report No AG-501 Not GLP Not Published Syngenta File N° CGA169374/0051	N	SYN
IIA 4.2.2.1/05	Kühne-Thu, H.	1986	CGA 169374, Determination of parent compound by gas chromatography, Plant material Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No REM-7-86 Not GLP Not Published Syngenta File N° CGA169374/0050	N	SYN
IIA 4.2.2.1/06	Kühne-Thu, H.	1997a	Determination of Metabolite CGA 205375 by HPLC-UV, Soil Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection AG, Basel, Switzerland, Report No REM 147.04 Not GLP Not Published Syngenta File N° CGA169374/1387	N	SYN
IIA 4.2.2.1/07 IIA 4.2.2.2/17	Formica, G	1992a	Determination of free 1,2,4-triazole by high performance liquid chromatography Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No REM-130-04 Not GLP Not Published Syngenta File N° CGA64250/2024	N	SYN

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IIA 4.2.2.1/08	Formica, G.	1992b	CGA 71818, Determination of total residues of CGA 71818 as 1,2,4-triazole by high performance liquid chromatography, soil, fruits Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No REM 107.06 Not GLP Not Published Syngenta File N° CGA71818/0942	N	SYN
IIA 4.2.2.2/02 IIA 4.2.2.2/11	Kühne-Thu, H.	1990a	Determination of residues of parent compound in soil after treatment with fungicide 'CGA169374 EC 250' Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No RR-2023-89 GLP Not Published Syngenta File N° CGA169374/0342	N	SYN
IIA 4.2.2.2/03 IIA 4.2.2.2/10	Kühne-Thu, H.	1990b	Determination of residues of parent compound in soil after treatment with fungicide 'CGA169374 EC 250' Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No RR-2024-89 Not GLP Not Published Syngenta File N° CGA169374/0341	N	SYN
IIA 4.2.2.2/05 IIA 4.2.2.2/12 IIA 4.2.2.2/19 IIA 4.2.2.2/20	Kühne-Thu, H.	2000	Long term study on fate and behaviour of Difenconazole (CGA 169374) in soil in Switzerland Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection AG, Basel, Switzerland, Report No 2031/89-98 GLP Not Published Syngenta File N° CGA169374/0652	Y	SYN
IIA 4.2.2.2/06	Kühne-Thu, H.	1990c	Determination of residues of parent compound in soil after treatment with 'Difenaconazole EC 250' - field experiment Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No RR-2097-89 Not GLP Not Published Syngenta File N° CGA169374/0335	N	SYN

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IIA 4.2.2.2/07	Kühne-Thu, H.	1990d	Determination of residues of parent compound in soil after treatment with 'Difenaconazole EC 250' - field experiment Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No 2096-89 Not GLP Not Published Syngenta File N° CGA169374/0336	N	SYN
IIA 4.2.2.2/08	Kühne-Thu, H.	1991a	Determination of residues of parent compound in soil after treatment with 'Difenaconazole EC 250' - Field experiment Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No 2040-89 Not GLP Not Published Syngenta File N° CGA169374/0337	N	SYN
IIA 4.2.2.2/09	Kühne-Thu, H.	1991b	Determination of residues of parent compound in soil after treatment with 'Difenaconazole EC 250' - field experiment Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No 2039-89 Not GLP Not Published Syngenta File N° CGA169374/0338	N	SYN
IIA 4.2.2.2/13	Kühne-Thu, H.	1992	Determination of residues difenoconazole in asparagus and soil - field trial - Italy Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No 2056-90 GLP Not Published Syngenta File N° CGA169374/0695	N	SYN
IIA 4.2.2.2/15	Tack, T.J.	1995	The determination of Difenoconazole (CGA 169374) residues in soil after successive applications of A7402G 250EC containing 250 g ai CGA 169374 applied as a foliar applicaion to winter wheat and bare soil for three years Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No CSTR 01:11 GLP Not Published Syngenta File N° CGA169374/1205	N	SYN

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IIA 4.2.2.2/16	Kühne-Thu, H.	1997b	Validation of Method REM 147.04: Validation by Analysis of Fortified Specimens and Determination of Recoveries; Extractability Test Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No 143/96 GLP Not Published Syngenta File N° CGA169374/1386	N	SYN
IIA 4.2.2.2/18	Sack, S	1994	Validation of methods: REM 3/86, 130.02, 230.04 and 130.06 Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No REM 3/86 GLP Not Published Syngenta File N° CGA64250/2345	N	SYN
IIA 4.2.3.1/01 IIA 4.2.3.2/01	Tribolet, R.	1990	CGA 169374, Determination of residues of parent compound by gas liquid chromatography (GLC), potable water Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No REM-147-01 Not GLP Not Published Syngenta File N° CGA169374/0055	N	SYN
IIA 4.2.3.1/02 IIA 4.2.3.2/02	Tribolet, R.	1999a	Determination of parent compound by gas chromatography, Water Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection AG, Basel, Switzerland, Report No REM 147.05 Not GLP Not Published Syngenta File N° CGA169374/1783	N	SYN
IIA 4.2.3.2/03	Tribolet, R.	1999b	Validation of Method REM 147.05 by Analysis of Fortified Water Specimens for Difenoconazole (CGA 169374) and Evaluation of Recoveries Novartis Crop Protection AG, Basel, Switzerland, Report No 226/98 GLP Not Published Syngenta File N° CGA169374/1782	N	SYN

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IIA 4.2.4.1/01 IIA 4.2.4.2/02	Tribolet, R.	1992	Sampling of air and determination of residues of parent compound by gas chromatography Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No REM-147-02 Not GLP Not Published Syngenta File N° CGA169374/0722	N	SYN
IIA 4.2.4.2/01	Tummon, O. J.	2004b	Difenoconazole. Validation of an Analytical Method for the Determination of Residues of Difenoconazole in Air Syngenta Crop Protection AG, Basel, Switzerland Syngenta, Jealott's Hill, United Kingdom, Report No RJ3495B GLP Not Published Syngenta File N° CGA169374/2500	Y	SYN
IIA 4.2.4.2/03	Tribolet, R.	1996	Report on Special Study 102/96. Validation of method REM 147.02 in air, Validation by analysis of fortified specimens and determination of recoveries Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, Report No 102/96 GLP Not Published Syngenta File N° CGA169374/1192	N	SYN
IIIA1 5.1.1/01	Käser, W.	1992	Analytical Method CGA 169374 in formulation (A-7402 G/H/K) Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Müncwilen AG, Müncwilen, Switzerland, Report No AF-1044/1 Not GLP Not Published Syngenta File N° CGA169374/1027	N	SYN
IIIA1 5.1.2/01	Käser, W.	1994	Report on validation of Analytical Method AF-1044/1 Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Müncwilen AG, Müncwilen, Switzerland, Report No 24393 GLP Not Published Syngenta File N° CGA169374/1028	N	SYN

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IIIA1 5.1.2/02	Krips, H.	1998a	Report on validation of analytical method - AF-1044/1 Novartis Crop Protection AG, Basel, Switzerland NOTOX B.V., 'S Hertogenbosch, Netherlands, Report No 235834 GLP Not Published Syngenta File N° CGA169374/1864	N	SYN
IIIA2 5.1.1/01	Kaerer, W.	1999	Analytical method CGA 169374 in A-9142 G (FS 030) by liquid chromatography Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland, Report No AF- 1385/1 Not GLP Not Published Syngenta File N° CGA169374/1779	N	SYN
IIIA2 5.1.2/01	Käser, W.	1999a	Report on validation of analytical method - AF-1385/1 Novartis Crop Protection AG, Basel, Switzerland Novartis Crop Protection Mönchwil AG, Mönchwil, Switzerland, Report No 72771 GLP Not Published Syngenta File N° CGA169374/2020	N	SYN

ⁱ Protection for 5 years claimed from date of decision concerning listing in Annex I - the study report has not been submitted any of the Member States in support of an application for authorization, or (though the study report has been submitted) has not been used any of the Member States as the basis for decision on the initial authorization, or to maintain a given authorization, of a plant protection product before the date of submission of the dossier to Rapporteur Member State.

ⁱⁱ Owners' code identifications and names (Code identification: SYN, Name: Syngenta Limited)