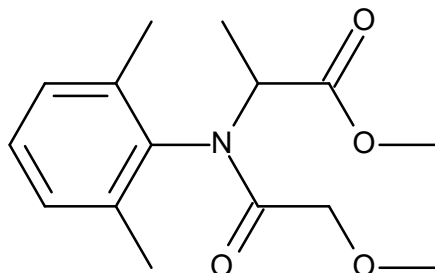


METALAXYL

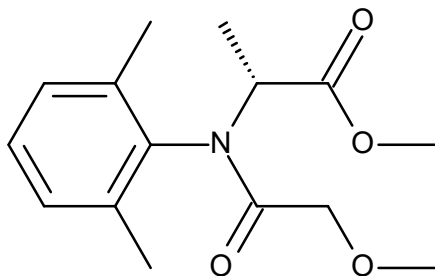
365



<i>ISO Common Name</i>	Metalaxyl
<i>Chemical Name</i>	methyl N-(2-methoxyacetyl)-N-(2,6-xylyl)-D-alaninate (IUPAC) DL-alanine, N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-, methyl ester (CAS)
<i>CAS Number</i>	57837-19-1
<i>Empirical formula</i>	C ₁₅ H ₂₁ N O ₄
<i>Molecular mass</i>	279.3
<i>m.p.</i>	71.8 - 72.3 °C
<i>b.p.</i>	101 °C
<i>v.p.</i>	0.29 mPa at 20°C
<i>Solubility</i>	In water 7.1 g/l; benzene 550 g/l; dichloromethane 750 g/l; n-hexane 9.1 g/l; methanol 650 g/l; octanol 270 g/l; propan-2-ol 270 g/l, all at 20 °C
<i>Stability</i>	<i>stable in neutral and acidic media at room temperature</i>
<i>Description</i>	colorless crystals
<i>Formulation</i>	suspension concentrates, water dispersible granules

METALAXYL-M

365



<i>ISO Common Name</i>	Metalaxyl-M
<i>Chemical Name</i>	<i>methyl N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-D-alaninate (IUPAC);</i> D-alanine, N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-, methyl ester (CAS)
<i>CAS Number</i>	70630-17-0
<i>Empirical formula</i>	C ₁₅ H ₂₁ N O ₄
<i>Molecular mass</i>	279.3
<i>v.p.</i>	3.3 mPa at 20°C
<i>Solubility</i>	In water 26 g/l; n-hexane 59 g/l; all at 20 °C
<i>Description</i>	yellow to brown liquid
<i>Formulation</i>	suspension concentrates, water dispersible granules
<i>Note</i>	Metalaxyl is the racemic mixture of the two enantiomers Metalaxyl-M is a mixture of the enantiomers (CGA329351 (R-enantiomer) major enantiomer and CGA351920 (S-enantiomer, minor enantiomer). The overall assay determination by GC can be used for both. The chiral method discriminates between Metalaxyl and Metalaxyl-M.

**METALAXYL and METALAXYL-
M TECHNICAL**
*YYY/TC/(M)/-

1 Sampling. Take at least 100 g.

2 Identity tests

2.1 Infrared. Prepare a film between sodium chloride plates and scan from 4000 to 650 cm^{-1} . The spectrum obtained from the sample should not differ significantly from that of the reference grade material.

2.2 GLC. Use the GLC method below. The relative retention time of Metalaxyl with respect to the internal standard for the sample solution should not deviate by more than 2% from that of the calibration solution.

3 Metalaxyl

OUTLINE OF METHOD

The sample of Metalaxyl technical material is dissolved in tert-butyl-methyl ether, containing an internal standard, and the Metalaxyl content determined (g/kg) by capillary gas chromatography.

REAGENTS

Metalaxyl-M: reference standard, of known purity.

Tert-butyl methyl ether (TBME): GC grade (for Technical and other Formulations)

Acetone: GC grade (for WG Formulations)

benzyl benzoate: Internal standard. Must not contain impurities with the same retention time as Metalaxyl or Metalaxyl-M.

Internal Standard Solution. Prepare a single stock of 10.0 mg/ml internal standard solution, of sufficient volume for all samples to be analyzed. For example, to prepare 200 ml stock solution, dissolve 2.0 g of benzyl benzoate in 200 ml TBME.

* CIPAC provisional method 2024. Based on a method supplied by Syngenta Crop Protection, Switzerland.

Calibration solution. Weigh (to the nearest 0.1 mg) 90 – 110 mg (*s* mg) of reference standard into a 50 ml volumetric flask. Add by pipette or calibrated dispenser, 5.0 ml of the internal standard stock solution and dilute to the mark with solvent. Place the flask in an ultrasonic apparatus for 5 minutes.

APPARATUS

Gas chromatograph equipped with a split/splitless injection and a flame ionisation detector.

Capillary column fused silica, length 30 m x 0.25 mm (i.d.), film thickness: 0.25 µm, coated with crosslinked dimethyl polysiloxane (DB-5 MS).

Ultrasonic bath

Electronic integrator or data system

PROCEDURE

(a) Gas chromatographic conditions (typical):

Column	fused silica, length 30 m x 0.25 (i.d.) mm, film thickness: 0.25 µm, coated with crosslinked dimethyl polysiloxane (DB-5 MS or equivalent).
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Ert-butyl methyl ether

Injector	split injection
Injection volume	1 µl
Split ratio	200 : 1

<i>Detector</i>	flame ionisation
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Temperatures

Injection port	250 °C
Detector	300 °C

Oven program

temp 1	160 °C,
ramp	rate 10 °C/min
temp 2	230 °C,
ramp	rate 50 °C/min
temp 3	300 °C, hold 7 min

Gas flow rates

Column H₂ (carrier), 1.5 ml/min, constant flow

Detector

Air 400 ml/min

Hydrogen 30 ml/min

Nitrogen (make up) 30 ml/min

Retention times

Metalaxyl approx. 5.70 min

Internal standard approx. 4.65 min (approximate)

(b) System equilibration. Prepare two calibration solutions. Inject 1 µl portions of solution C_A until the response factors (*f_i*) obtained for two consecutive injections differ by less than 1.0 %. Then inject a 1 µl portion of the solution C_B. The response factor, *f_i*, for this solution should not deviate by more than 1.0 % from that of solution C_A, otherwise prepare new calibration solutions. If the peak retention times differ significantly from the approximate values quoted, then the flow rate may be adjusted accordingly.

(c) Sample preparation. Prepare solutions in duplicate for each sample. Weigh (to the nearest 0.1 mg) sufficient sample to contain 90-110 mg (w mg) of Metalaxyl into a suitable container (50 ml volumetric flask). Add by pipette or calibrated dispenser 5.0 ml of the internal standard solution to the weighed aliquot. Dilute to the mark with solvent. Cap the container and sonicate for 5 min (solutions S_A and S_B).

(d) Determination. Inject in duplicate 1 µl portions of each sample solution bracketing them with duplicate injections of the calibration solution as follows: calibration solution C_A, calibration solution C_B, calibration solution C_A, sample solution S1_A, sample solution S1_B, calibration solution C_A, sample solution S2_A, sample solution S2_B, calibration solution C_A, and so on for further samples. Measure the relevant peak areas. If the peak shapes and precision of analysis deteriorate, this may indicate the build-up of formulation residue in the GC, necessitating maintenance of injection ports. Consider replacing injection liners, gold seals and/or split vent lines.

(e) Calculation. Calculate the mean value of each pair of calibration response factors, bracketing the two injections of a sample, and use this value for calculating the Metalaxyl contents of the bracketed sample injections.

$$f_i = \frac{I_r \times s \times P}{H_s}$$

$$\text{Content of Metalaxyl} = \frac{f \times H_w}{I_q \times w} \text{ (g/kg)}$$

where:

f_i = individual response factor

f = mean response factor

H_s = peak area of Metalaxyl in the calibration solution

H_w = peak area of Metalaxyl in the sample solution

I_r = peak area of the internal standard in the calibration solution

I_q = peak area of the internal standard in the sample solutions

s = mass of Metalaxyl reference standard in the calibration solution (mg)

w = mass of sample taken (mg)

P = purity of Metalaxyl reference standard (g/kg)

Repeatability r = added after ring trial

Reproducibility R = added after ring trial

METALAXYL SUSPENSION CONCENTRATES
***YYY/SL AND**
ES/(M)-

1 Sampling. Take at least 500 ml.

2 Identity tests

2.1 Infrared As for Metalaxyl technical YYY/TC/(M)/2.1 and Fig 1.

2.2 GLC As for Metalaxyl technical YYY/TC/(M)/2.2 and Fig 2.

3 Metalaxyl. As for Metalaxyl technical YYY/TC/(M)/3 except:

APPARATUS

Sample filtering device with a membrane filtration unit compatible with organic solvents and a 0.45µm pore diameter.

PROCEDURE

(c) Sample preparation. Prepare solutions in duplicate for each sample. Homogenize the test sample thoroughly. Weigh (to the nearest 0.1 mg) sufficient sample to contain 90 – 110 mg (*w* mg) of Metalaxyl (equal to 200 – 240 mg Metalaxyl formulation SL 480) into a suitable container (50 ml flask or bottle). Add by pipette or calibrated dispenser 5.0 ml of the internal standard solution to the weighed aliquot and dilute to the mark with solvent. Cap the container and sonicate for 10 min (solutions S_A and S_B). Filter solutions through a 0.45 µm filter prior to analysis (solutions S_A and S_B).

Repeatability r = added after ring trial

Reproducibility R = added after ring trial

* CIPAC provisional method 2022. Based on a method supplied by Syngenta Crop Protection Switzerland.

METALAXYL WATER DISPERSIBLE GRANULES

*YYY/WG/(M)/-

- 1 **Sampling.** Take at least 500 g.
- 2 **Identity tests**
 - 2.1 **Infrared.** As for Metalaxyl technical YYY/TC/(M)/2.1 and Fig 1.
 - 2.2 **GLC.** As for Metalaxyl technical YYY/TC/(M)/2.2 and Fig 2.
- 3 **Metalaxyl.** As for Metalaxyl technical YYY/TC/M/3.

APPARATUS

Sample filtering device with a membrane filtration unit compatible with organic solvents and a 0.45 µm pore diameter.

PROCEDURE

Internal Standard Solution. Prepare a single stock of 1.0 mg/ml internal standard solution, of sufficient volume for all samples to be analyzed. For example, to prepare 500 ml stock solution, dissolve 0.525 g of benzyl benzoate in 500 ml Acetone.

Calibration solution. Weigh (to the nearest 0.1 mg) 50 – 55 mg (*s* mg) of reference standard into a 100 ml Erlenmeyer flask. Add by pipette or calibrated dispenser, 50.0 ml of the internal standard stock solution. Add 3.0 ml of water and 20g molecular sieve (0.3 nm). Shake the mixture and wait 20 minutes.

Sample preparation. Prepare solutions in duplicate for each sample. Homogenize the test sample thoroughly. Weigh (to the nearest 0.1 mg) sufficient sample to contain 50 – 55 mg (*w* mg) of Metalaxyl (equal to 1250 – 1350 mg Metalaxyl formulation WG 4) into a suitable container (200 ml flask or bottle). Add 3.0 ml of water and treat the mixture with ultrasound for 5 minutes. Add by pipette or calibrated dispenser 50.0 ml of the internal standard solution. Cap the container and sonicate again for 10 min (solutions S_A and S_B). Add 20g molecular sieve (0.3 nm) shake well and allow the mixture to stand for 20 minutes. Filter solutions through a 0.45 µm filter prior to analysis (solutions S_A and S_B).

* CIPAC provisional method 2022. Based on a method supplied by Syngenta Crop Protection Switzerland.

Repeatability r = added after ring trial
Reproducibility R = added after ring trial

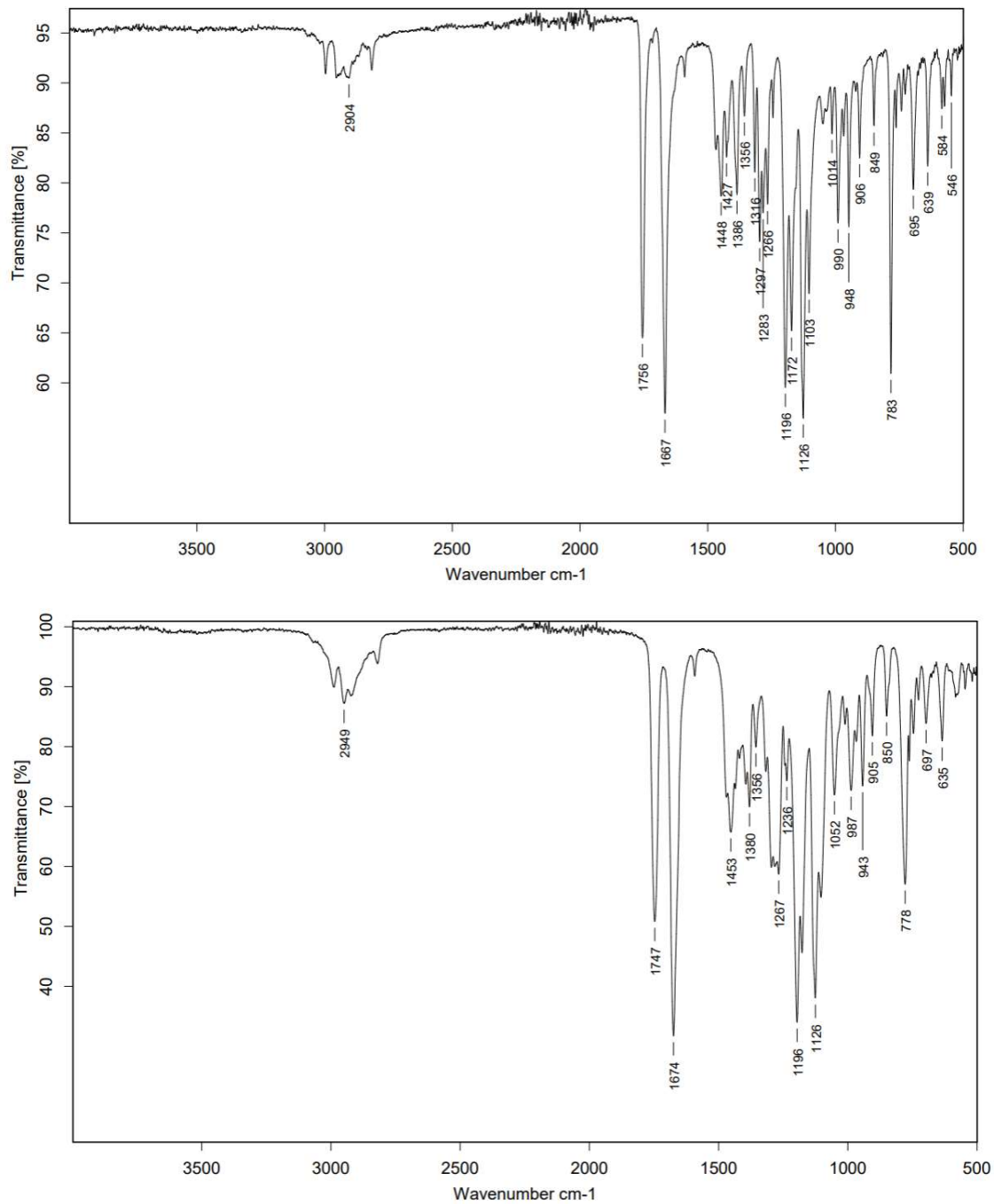


Fig. 1 Typical IR spectrum of Metalaxyl (upper) and Metalaxyl-M tech. (lower) according to xxx/TC/M/2.1

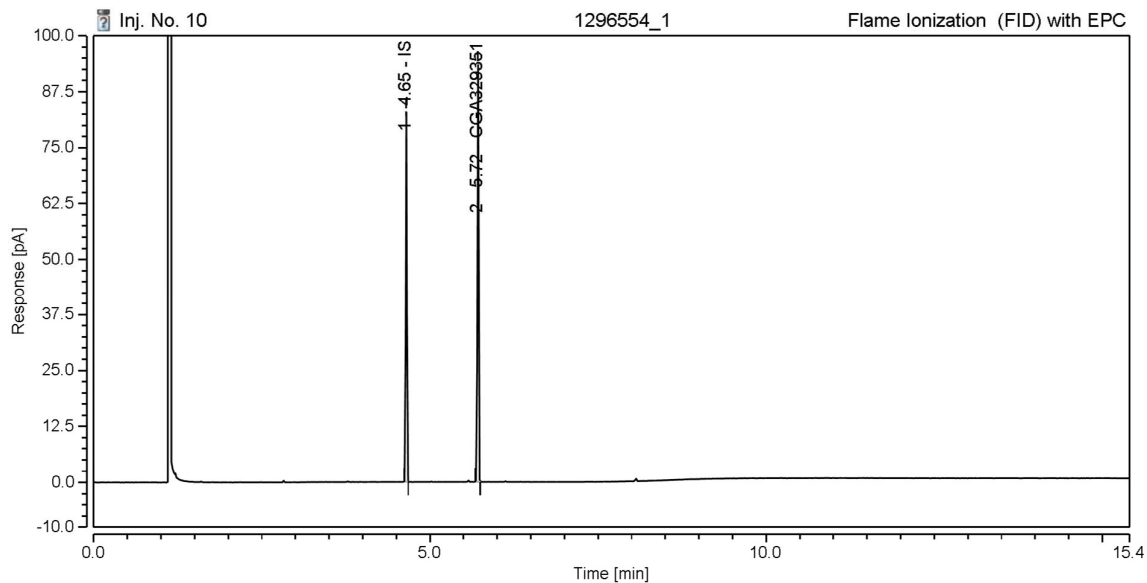


Fig. 2 Typical chromatogram of Metalaxyl TC

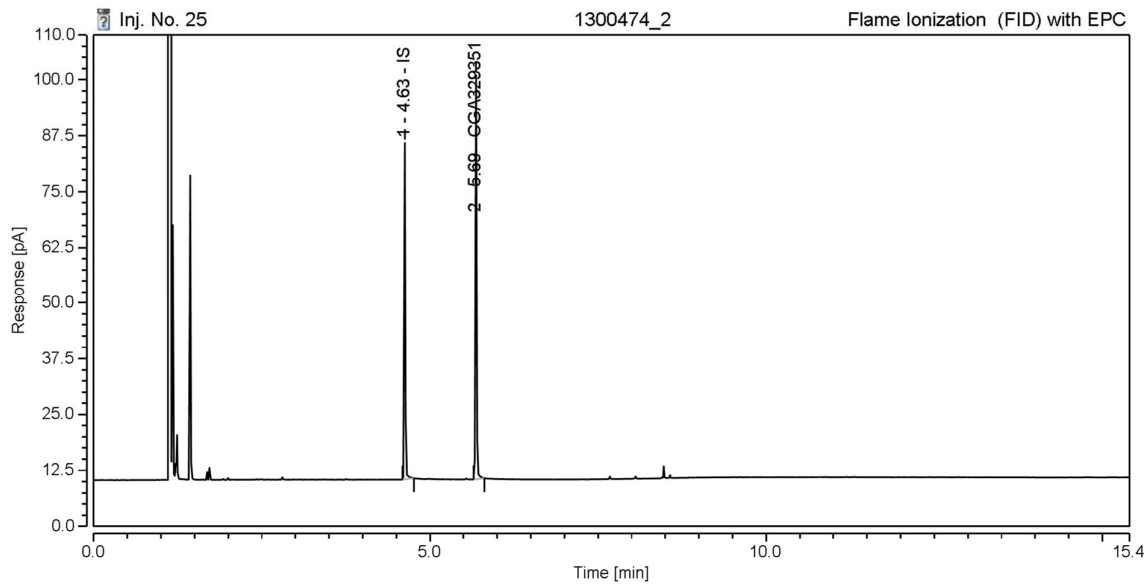


Fig. 3 Typical chromatogram of Metalaxyl in SL

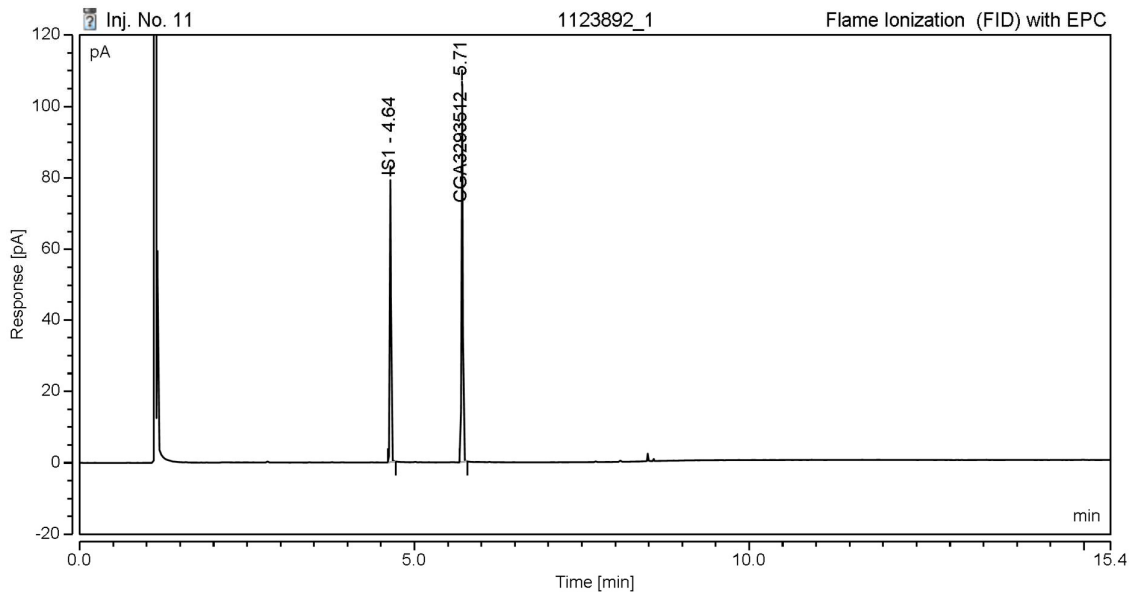


Fig. 4 Typical chromatogram of Metalaxyl in ES

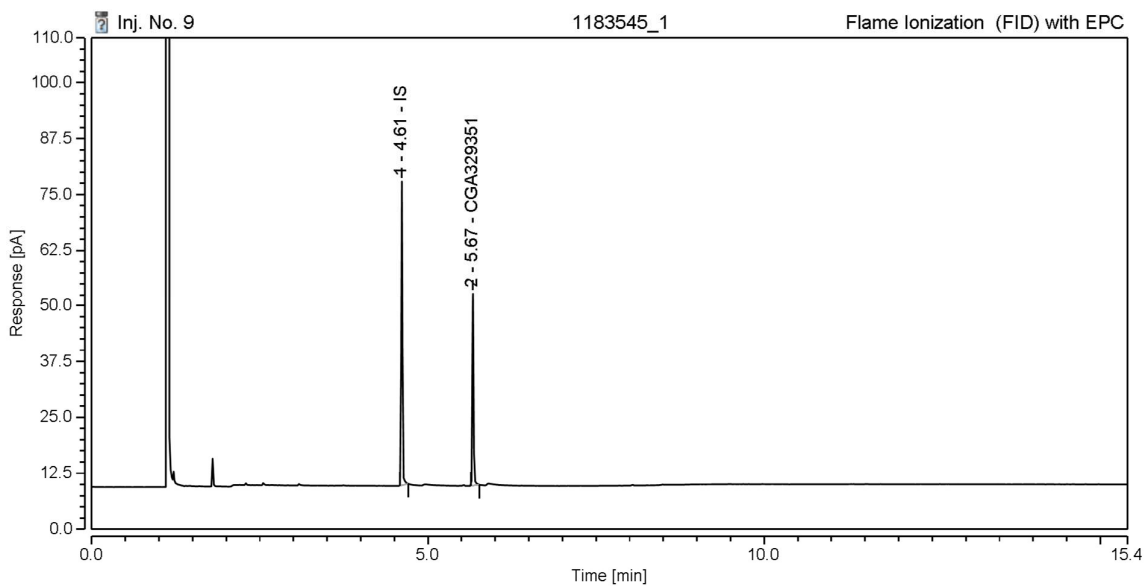


Fig. 5 Typical chromatogram of Metalaxyl in WG

**METALAXYL-M TECHNICAL
CHIRAL
*YYY/TC/(M)/-**

1 Sampling. Take at least 100 g.

2 Identity tests

2.1 HPLC. Use the HPLC method below. The relative retention time of the respective peak in the sample solution should not deviate by more than 2% from that of the calibration solution.

3 Metalaxyl-M

OUTLINE OF METHOD

The sample of Metalaxyl or Metalaxyl-M technical material is dissolved in acetonitrile and separated by high performance liquid chromatography on a Chiralpak IB column with a mixture of acetonitrile/water as eluent. A UV-detector is used at 220 nm. The content of the single isomers is determined by area%.

REAGENTS

Metalaxyl-M: reference standard, of known purity.

Acetonitrile: HPLC grade

water

Calibration solution (only for identification). Weigh (to the nearest 0.1 mg) 35 – 45 mg (*s* mg) of reference standard into a 100 ml volumetric flask. Add 80 ml acetonitrile and place the flask in an ultrasonic apparatus for 5 minutes. Allow the mixture to reach ambient temperature and fill to the mark with acetonitrile.

* CIPAC provisional method 2024. Based on a method supplied by Syngenta Crop Protection, Switzerland.

APPARATUS

High performance liquid chromatograph

Ultrasonic bath

HPLC column Chiralpak IB 150 x 4.6 mm (i.d.), 5 µm particle size

Electronic integrator or data system

PROCEDURE

(a) Liquid chromatographic conditions (typical):

Column 150 x 4.6 mm (i.d.) packed with Chiralpak IB, 5 µm particle size

Column Temperature 40 °C

Flow rate: 0.8 ml/min

Injection Volume 10 µl

Detector Wavelength 220 nm

Run time 28 minutes

Operating conditions

Eluent A water/acetonitrile (65/35, v/v)

Eluent B acetonitrile

Gradient

Time (min)	A	B
0	100	0
10	100	0
11	20	80
20	20	80
21	100	0
28	100	0

Retention times

CGA351920 (S-enantiomer)	approx. 7.38 min
CGA329351 (R-enantiomer)	approx. 8.54 min

(b) System equilibration. Inject 10 µl of the sample solution until the retention time of CGA329351 (R-enantiomer) obtained for two consecutive chromatograms differ from one another by not more than 2%.

(c) Sample preparation. Prepare solutions in duplicate for each sample. Weigh (to the nearest 0.1 mg) sufficient sample to contain 35-45 mg (w mg) of Metalaxyl-M into a suitable container (100 ml volumetric flask). Add acetonitrile, cap the container and sonicate for 5 min (solutions S_A and S_B). Fill to the mark with acetonitrile. Measure sample solution within 24 hours.

(d) Determination. Inject 10 µl of the sample solution and determine the respective peak areas.

(e) **Calculation.** Calculate the individual isomer as follows:

$$\%CGA351920(S - enantiomer) = \frac{F_S \times C}{F_R + F_S}$$

F_R = Peak area of CGA329351 (R-enantiomer) on the test chromatogram

F_S = Peak area of CGA351920 (S-enantiomer) on the test chromatogram

C Content of metalaxyl-M (incl. its S-enantiomer), section 2 in % w/w

$$\%CGA329351(R - enantiomer) = \frac{F_R \times C}{F_R + F_S}$$

F_R = Peak area of CGA329351 (R-enantiomer) on the test chromatogram

F_S = Peak area of CGA351920 (S-enantiomer) on the test chromatogram

C Content of metalaxyl-M (incl. its S-enantiomer), section 2 in % w/w

Repeatability r = added after ring trial

Reproducibility R = added after ring trial

METALAXYL-M CHIRAL EMULSIFIABLE CONCENTRATES
***YYY/SL AND ES/(M)-**

1 Sampling. Take at least 500 ml.

2 Identity tests

2.1 HPLC use the reversed phase HPLC as described below.

3 Metalaxyl-M. As for Metalaxyl-M technical chiral YYY/TC/(M)/3 except:

APPARATUS

Sample filtering device with a membrane filtration unit compatible with organic solvents and a 0.45µm pore diameter.

PROCEDURE

(c) Sample preparation. Prepare solutions in duplicate for each sample. Homogenize the test sample thoroughly. Weigh (to the nearest 0.1 mg) sufficient sample to contain 35 – 45 mg (*w* mg) of Metalaxyl-M (equal to 80 – 100 mg Metalaxyl-M formulation SL 480) into a suitable container (100 ml flask or bottle). Add acetonitrile, cap the container and sonicate for 10 min (solutions S_A and S_B). Fill to the mark with acetonitrile. Filter solutions through a 0.45 µm filter prior to analysis (solutions S_A and S_B). Measure sample solution within 24 hours.

Repeatability r = added after ring trial

Reproducibility R = added after ring trial

* CIPAC provisional method 2022. Based on a method supplied by Syngenta Crop Protection Switzerland.

METALAXYL-M CHIRAL WATER DISPERSIBLE GRANULES
***YYY/WG/(M)/-**

1 Sampling. Take at least 500 ml.

2 Identity tests

2.1 HPLC use the reversed phase HPLC as described below.

3 Metalaxyl-M. As for Metalaxyl-M technical chiral YYY/TC/(M)/3 except:

APPARATUS

Sample filtering device with a membrane filtration unit compatible with organic solvents and a 0.45µm pore diameter.

PROCEDURE

(c) Sample preparation. Prepare solutions in duplicate for each sample. Homogenize the test sample thoroughly. Weigh (to the nearest 0.1 mg) sufficient sample to contain 35 – 45 mg (*w* mg) of Metalaxyl-M (equal to 900 – 1100 mg Metalaxyl-M formulation WG 4) into a suitable container (100 ml flask or bottle). Add 10 ml water and sonicate for 5 min. Add 60 ml acetonitrile, cap the container and sonicate again for 10 min (solutions S_A and S_B). Fill to the mark with acetonitrile. Filter solutions through a 0.45 µm filter prior to analysis (solutions S_A and S_B). Measure sample solution within 24 hours.

Repeatability r = added after ring trial

Reproducibility R = added after ring trial

* Draft method. Based on a method supplied by Syngenta Crop Protection Switzerland.

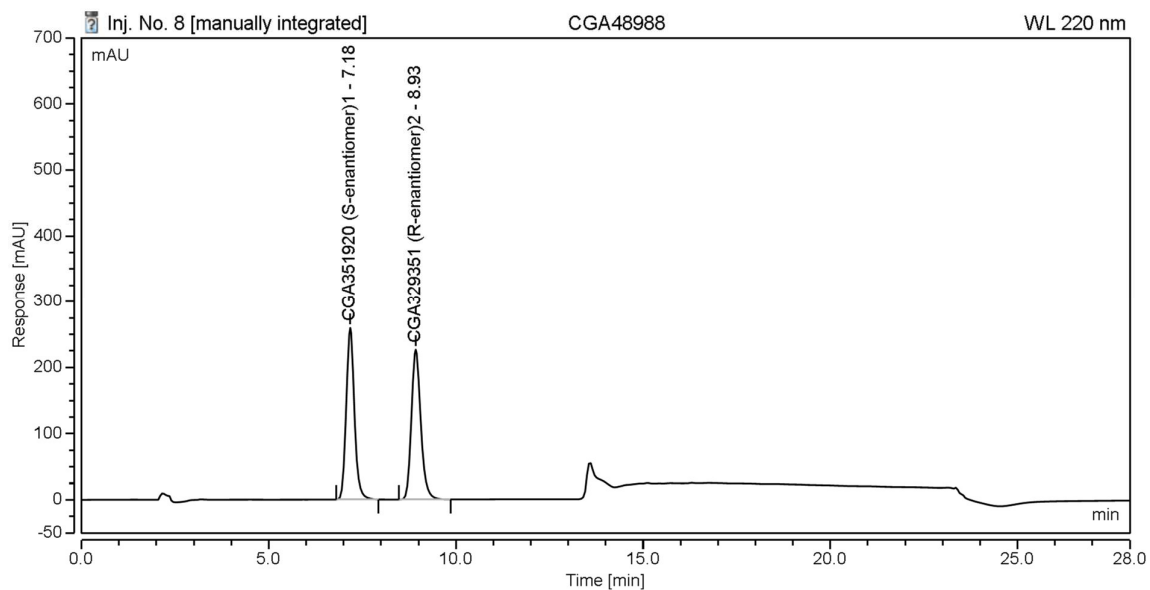


Fig. 6 Typical chromatogram of Metalaxyl TC/M/2.1

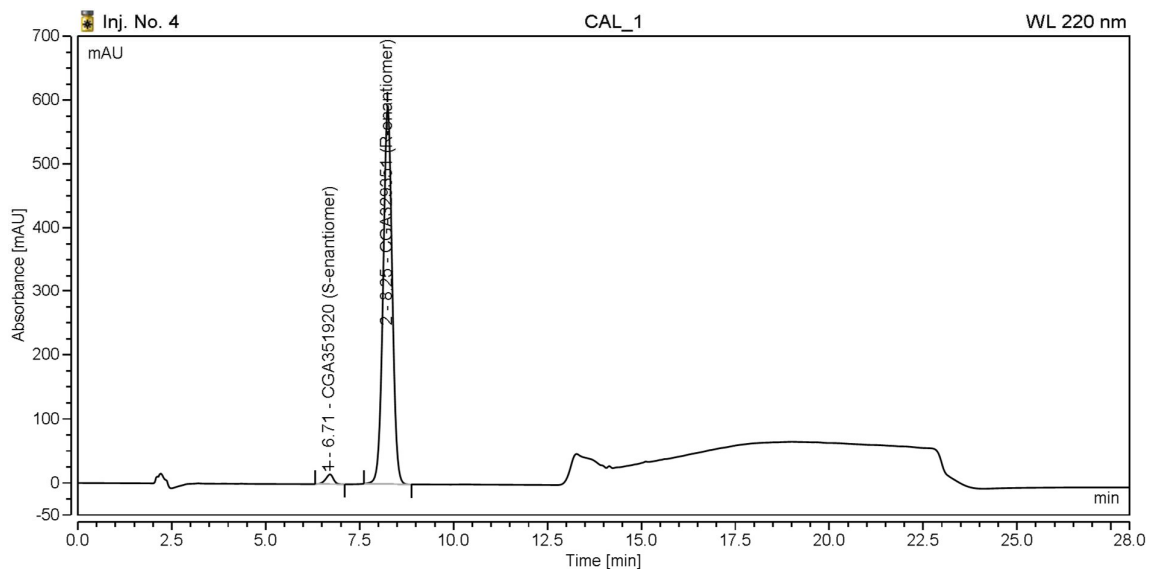


Fig. 7 Typical chromatogram of Metalaxyl-M TC chrial

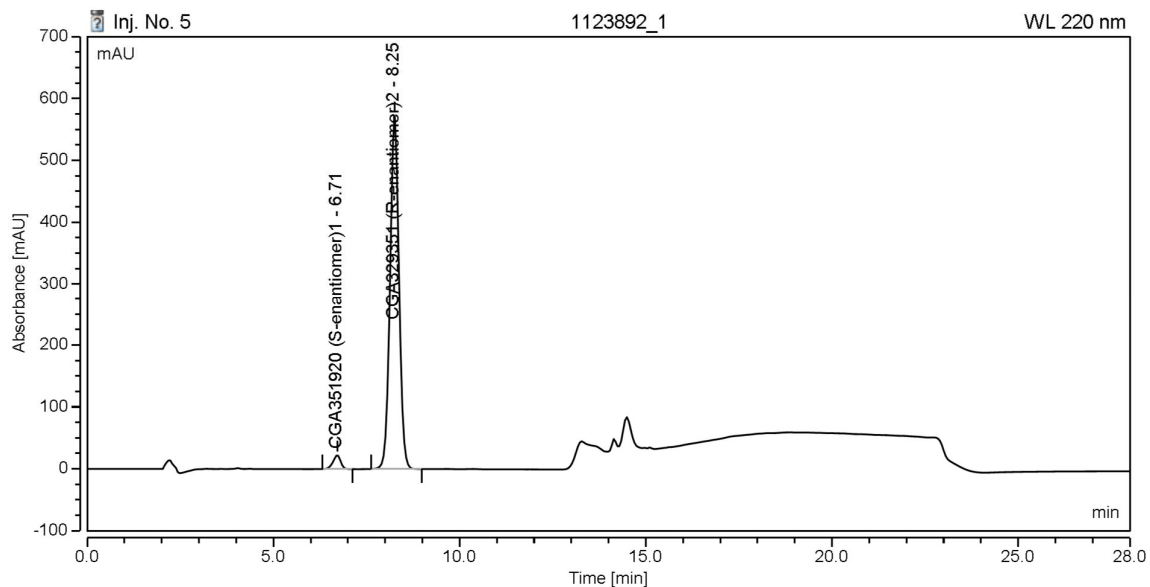


Fig. 8 Typical chromatogram of Metalaxyl-M chiral in ES

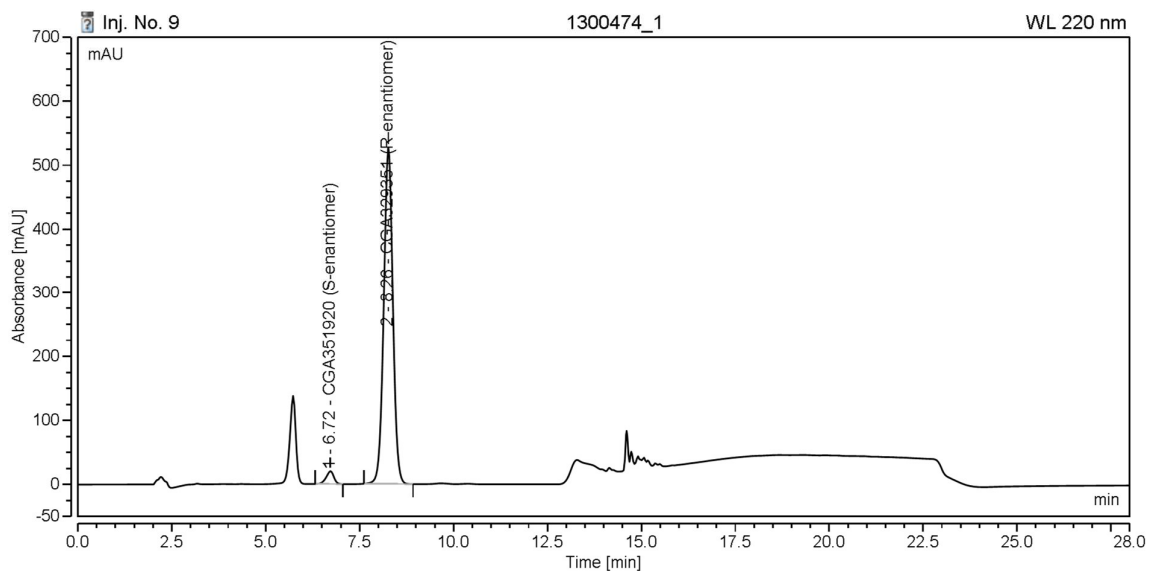


Fig. 9 Typical chromatogram of Metalaxyl-M chiral in SL

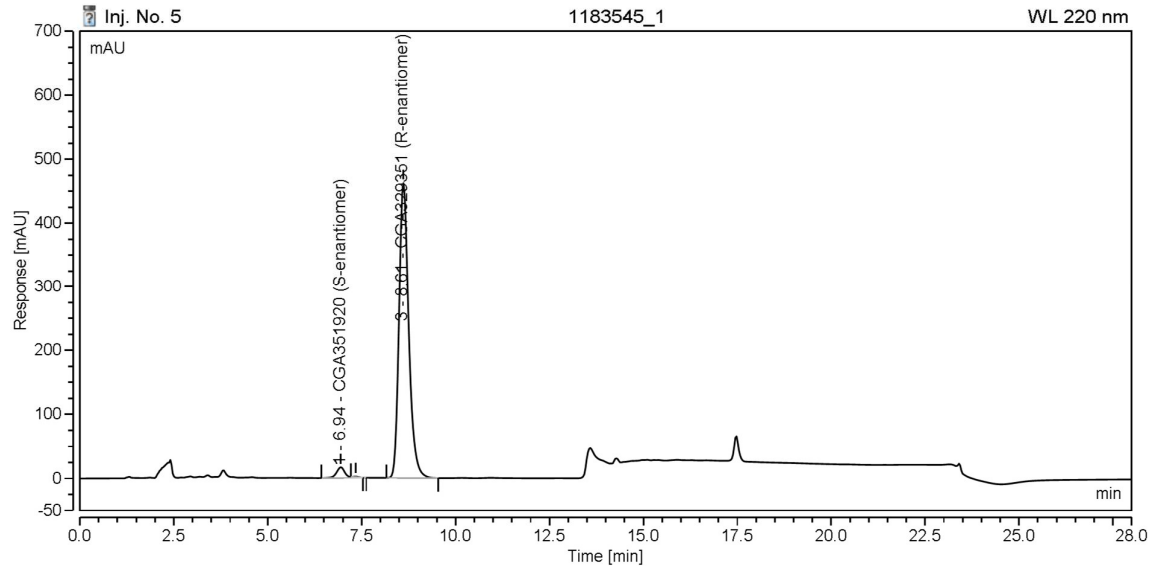


Fig. 10 Typical chromatogram of Metalaxyl-M chiral in WG