



Draft Assessment Report

Evaluation of Active Substances

Plant Protection Products

Prepared according to **Regulation (EC) 1107/2009**
as it applies in Great Britain (GB PPP)

Cinmethylin (BAS 684 H)

Volume 3 – B.5 (PPP) – BAS 684 03 H

Methods of Analysis

Great Britain

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Version History

When	What
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B.5. METHODS OF ANALYSIS

B.5.1. METHODS USED FOR THE GENERATION OF PRE-AUTHORISATION DATA

B.5.1.1. Analysis of the plant protection product

(a) Methods for the determination of the active substance and/or variant in the plant protection product

Reference: KCP 5.1.1/01
Title: Determination of Cinmethylin in EC formulations by means of GC
Author: Muenz J.; 2017a
Report No.: 2017/1121786
Guidline(s): None
GLP: No
Acceptability: Yes

Reference: KCP 5.1.1/03
Title: Determination of Cinmethylin in EC formulations by means of GC
Author: Muenz J.; 2017b
Report No.: 2017/1121789
Guidline(s): US EPA OPPTS Harmonized Test Guideline 830.1800, SANCO/3030/99 rev. 4 (11 July 2000), ABNT NBR 14029
GLP: Yes
Acceptability: Yes

Reference items

BAS 684 03 H: Batch No. FD-170209-0001, (741.0 g/L cinmethylin), expiry date 01/03/2018, CoA provided.
Cinmethylin: Batch No. L87-84, purity 99.0 % BASF, expiry date 01/08/17, CoA provided.
Triphenyl phosphate: Batch No. BCBM3828V, purity 99 % Allessa GmbH, no expiry date stated, CoA provided.
BAS 684 AT H: Blank formulation (without cinmethylin).

Sample preparation

Approximately 160 mg of test item (± 15 mg) were weighed exactly into a 50 mL volumetric flask and 2 mL of internal standard stock solution were added. After homogenisation, the flask was made up to the mark with acetonitrile and the solution filtered through a 0.20 μ m syringe filter.

Analytical method AFL0954/01

Samples were analysed by high resolution gas chromatography (HR-GC) with split injection and flame ionisation detection (FID). Quantification is carried out using triphenyl phosphate as an internal standard. The following conditions were noted:

System 1

GC System	Agilent 6890
Injector	Agilent 7683 Series
Detector	FID
Data system	Dionex Chromeleon, version 6.80.
Injection	Split
Column	DB-1701, 30 m length; 0.32 mm I. D.; 0.25 μ m film thickness, Agilent
Carrier Gas	Helium 4.6
Carrier Gas Flow	2.5 mL/min, constant flow
Make-up Gas	Nitrogen 5.0
Make-up Gas Flow	34 mL/min
Detector Gas	Hydrogen
Detector Gas Flow	33 mL/min

Detector Temperature	300 °C		
Injector Temperature	250 °C		
Column Temperature Program	Temperature [°C]	Hold time [min]	Heating Rate [°C/min]
	40	2	30
	210	1	20
	290	5	-
Total Run Time	18 min		
Injection Volume	1 µL		
Injection Split Ratio	1:10		
Split Gas Flow	25 mL/min		
System 2			
GC System	Varian 3800		
Detector	Varian 1200L		
Data System:	Varian MS Workstation, Version 6.9		
Injector Split	Split ratio 1:100		
Column	DB-1701, 30 m length; 0.32 mm I. D.; 0.25 µm film thickness, Agilent		
Carrier Gas	Helium 4.6		
Carrier Gas Flow	1.8 mL/min, constant flow		
Detector Temperature	230 °C		
Injector Temperature	250 °C		
Column Temperature Program	Temperature [°C]	Hold time [min]	Heating Rate [°C/min]
	40	2	30
	210	1	20
	290	5	-
Injection Volume	0.5 µL		
Detection Voltage	1000 V		
Interface Temperature	290 °C		
Ionisation Mode	EI+, 70 eV		
Scan Range	TIC, m/z 35 - 400 (Da)		

Specificity

The chromatograms did not show any interference at the signal of cinmethylin or any other signals from the solvent, internal standard, test item and reference items. The retention times for cinmethylin in the reference and test samples were identical. The identity was confirmed by GC-MS analysis of test item and cinmethylin reference samples.

Linearity

The linear range for the determination of cinmethylin in the formulation BAS 684 03 H was assessed by duplicate injection of five individually diluted solutions containing cinmethylin in the range of 1.01 - 4.03 g/L. These concentrations correspond to contents of Cinmethylin in formulations BAS 684 03 H in the range of approx. 31.5 % to a hypothetical value of approx. 126 %.

The response was linear with a correlation coefficient of $r = 0.999489$ ($y = 1.1747 x + 0.1629$).

Precision (Repeatability)

Repeatability data was generated in duplicate from five sample determinations of BAS 684 03 H (Batch FD-170209-0001). The relative standard deviations (RSD) obtained were within the guideline requirements and the results are presented in Table 5.1.1/01 below.

Table 5.1.1/01 Precision Data

Concentration	Number of Samples	Mean Content (% w/w)	RSD (%)	Acceptable RSD (%)*
750 g/L	5	99.2	0.3	1.40
750 g/L	5	97.5	0.4	1.40

* Using modified Horwitz equation

Accuracy (Recovery)

Recovery data were generated from five samples of blank formulation fortified at approximately 80, 100 and 120 % of the nominal (750 g/L) concentration. The mean recoveries obtained for each fortification level were within the guideline requirements and the results are presented in Table 5.1.1/02 below.

Table 5.1.1/02 Recovery data

Fortification Level (g/kg)	Number of Samples	Mean Recovery (%)	RSD (%)
600	5	98.4	0.5
750	5	98.7	0.8
900	5	98.5	0.2

Limit of Quantification (LOQ)

Not required.

Conclusion

The analytical method is fully validated in accordance with SANCO/3030/99 rev. 4 for the determination of the active substance cinmethylin in the formulation BAS 684 03 H *via* GC-FID with GC-MS confirmation.

(b) Methods for determination of relevant impurities identified in the technical material or which may be formed during manufacture of the plant protection product or from degradation of the plant protection product during storage

It was stated by the applicant that no relevant impurities are identified in the formulation BAS 684 03 H. However, based on the identity and technical specification data included in the confidential section Volume 4 (C.1.2.3), two relevant impurities have been identified in cinmethylin technical material:

Toluene: Maximum 0.5 g/kg

BAS 4539586 (1SR,2RS,4RS)-1-methyl-4-(pro-pan-2-yl)-7-oxa-bicyclo[2.2.1]-heptan-2-ol: Maximum 4 g/kg

Analytical methods for the determination of these impurities in the formulation are therefore required.

Reference: KCP 5.1.1/06
Title: Determination of the solvents Toluene and o-Xylene in EC formulations containing Cinmethylin by means of Headspace GC
Author: Tolle S., 2016 a
Report No.: 2016/1296122
Guideline(s): None
GLP: No
Acceptability: Yes

Reference: KCP 5.1.1/07
Title: Validation of an analytical method for the determination of the solvents Toluene and o-Xylene in EC formulations containing Cinmethylin by means of Headspace GC
Author: Bacher R., 2017 b
Report No.: 2016/1296123
Guideline(s): US EPA OPPTS Harmonized Test Guideline 830.1800, SANCO/3030/99 rev. 4 (11 July 2000), ABNT NBR 14029
GLP: Yes
Acceptability: Yes

Reference:	KCP 5.1.1/05
Title:	Additional validation to the analytical method for the determination of the solvents Toluene and o-Xylene in EC-formulations containing Cinmethylin by means of Headspace GC for BAS 684 03 H
Author:	Bacher R., 2017 a
Report No.:	2017/1077862
Guideline(s):	US EPA OPPTS Harmonized Test Guideline 830.1800, SANCO/3030/99 rev. 4 (11 July 2000), ABNT NBR 14029
GLP:	Yes
Acceptability:	Yes

Note : The method was fully validated using the formulation BAS 684 02 H in study Bacher R., 2017 b . Addition validation data for BAS 64 03H were provided in study Bacher 2017a.. Comparison of composition of the two formulations is given in section C.1.4.1 of Vol 4.

Reference items

BAS 684 02 H: Batch No. FD-150416-0012, (737.6 g/L cinmethylin), expiry date 01/03/2017, CoA provided.
 BAS 684 03 H: Batch No. FD-170209-0001, (741.0 g/L cinmethylin), expiry date 01/03/2018, CoA provided.
 Toluene: Batch No1027B, purity 99.9 % BASF, CoA provided.
 o-xylene: Batch No. S7152797, purity 98.5 %, CoA provided.
 BAS 684 AE H: Blank formulation (without cinmethylin).
 BAS 684 AT H: Blank formulation (without cinmethylin).
 Internal standard: 100 mg/L iso-octane in dimethylsulfoxide (DMSO)

Sample preparation

Approximately 100 mg of test item was weighed into a 20 mL headspace vial and 1 mL of internal standard stock solution were added. The headspace via is sealed and transferred to the instrument autosampler.

Analytical method AFL0941/01

Samples were analysed by gas chromatography (GC) with headspace injection and flame ionisation detection (FID). Quantification is carried out using iso-octane as an internal standard. The following conditions were noted:

GC System	Agilent 6890		
Headspace Injector:			
Volume	400 µL		
Incubation temperature	85 °C		
Incubation time	10 min		
Syringe temperature	90 °C		
Flush time	20 s		
Agitator on time	2 s		
Agitator off time	2 s		
Filling speed	100 µL/s		
Injection speed	25000 µL/min		
Inlet temperature			
Column	DB-624, 30 m length; 0.25 mm I. D.; 1.4 µm film thickness, Agilent		
Carrier Gas	Helium		
Carrier Gas Flow	1.5 mL/min, constant flow		
Detector	FID		
Detector Temperature	280 °C		
Column Temperature Program	Temperature [°C]	Hold time [min]	Ramp Rate [°C/min]
	45	8	20
	200	3	-
Total Run Time	18.8 min		

Specificity

The chromatograms did not show any interference at the signal of toluene or any from the solvent, internal standard, test item and reference items. The retention times for toluene in the reference and test samples were identical. The identity was confirmed by GC-MS analysis of test item and toluene reference samples.

Linearity

The linear range for the determination of toluene in the formulation BAS 684 03 H was assessed by single injection of six solutions containing toluene in the range of 5.0 - 200 mg/L. These concentrations correspond to contents of toluene of approx. 68 to 2720 mg/kg toluene in the formulation.

The response was linear with a correlation coefficient of $r = 0.9977$ ($y = 0.00156734 x - 0.00304124$).

Precision (Repeatability)

Repeatability data was generated from seven sample determinations of BAS 684 02 H (Batch FD-170209-0001). In addition, seven samples of the BAS 684 02 H formulation (code BAS 684 AE H) were fortified with toluene at three different concentrations (i.e. seven samples per concentration). The relative standard deviations (RSD) obtained were within the guideline requirements and the results are presented in Table 5.1.1/03 below.

Table 5.1.1/03 Precision Data

Concentration (relative to cinnethylin content)	Number of Samples	RSD (%)	Acceptable RSD (%) [*]
0.488 g/kg	7	2.5	4.21
0.25 g/kg (fortified)	7	3.24	4.67
1 g/kg (fortified)	7	1.06	3.79
5 g/kg (fortified)	7	1.98	2.97

^{*} Using modified Horwitz equation

Accuracy (Recovery)

Recovery data were generated from seven samples of the blank BAS 684 02 H formulation (code BAS 684 AE H) fortified at 0.25 g/kg, 1 g/kg and 5 g/kg relative to the cinnethylin content. In addition, three samples of the blank BAS 684 03H (code BAS 684 AT H) were fortified at 0.25 g/kg relative to the cinnethylin content. The mean recoveries obtained for each fortification level were within the guideline requirements and the results are presented in Table 5.1.1/04 below.

Table 5.1.1/04 Recovery data

Fortification Level (relative to cinnethylin content)	Number of Samples	Mean Recovery (%)	RSD (%)
0.25 g/kg (BAS 684 02 H)	7	100	3.24
1.0 g /kg (BAS 684 02 H)	7	86	1.06
5.0 g /kg (BAS 684 02 H)	7	94	1.98
0.25 g/kg (BAS 684 03 H)	3	110	1.02

Limit of Quantification (LOQ)

0.25 g/kg relative to the cinnethylin content (i.e. approx. 0.18 mg/L in the formulation).

Conclusion

The analytical method is fully validated in accordance with SANCO/3030/99 rev. 4 for the determination of the impurity toluene in the formulation BAS 684 02 H *via* headspace GC-FID with GC-MS confirmation. Additional validate data were provided to show that the method is also applicable to the formation BAS 684 03 H.

No methods are currently available for the determination of the impurity BAS 4539586 in the formulation. These are required.

(c) Methods for determination of relevant co-formulants or components of co-formulants, where required by the national competent authorities

No methods are required for co-formulants or the components of co-formulants. These ingredients are not considered toxicologically or eco-toxicologically relevant at the concentrations present in the formulation

B.5.1.2. Methods for the determination of residues

B.5.1.2.1. In soil, water, sediment, air and any additional matrices used in support of environmental fate studies

All relevant methods are reported in Volume 3 CA B.5.1.2 of this DAR.

B.5.1.2.2. In soil, water and any additional matrices used in support of efficacy studies

All relevant methods are reported in Volume 3 CA B.5.1.2 of this DAR.

B.5.1.2.3. In feed, body fluids and tissues, air and any additional matrices used in support of toxicological studies

All relevant methods are reported in Volume 3 CA B.5.1.2 of this DAR.

B.5.1.2.4. In body fluids, air, and any additional matrices used in support of operator, worker, resident and bystander exposure studies

All relevant methods are reported in Volume 3 CA B.5.1.2 of this DAR.

B.5.1.2.5. In or on plants, plant products, processed food commodities, food of plant and animal origin, feed and any additional matrices used in support of residues studies

All relevant methods are reported in Volume 3 CA B.5.1.2 of this DAR.

B.5.1.2.6. In soil, water, sediment, feed and any additional matrices used in support of ecotoxicology studies

All relevant methods are reported in Volume 3 CA B.5.1.2 of this DAR.

B.5.1.2.7. In water, buffer solutions, organic solvents and any additional matrices resulting from the physical and chemical properties tests

All relevant methods are reported in Volume 3 CA B.5.1.2 of this DAR.

B.5.2. METHODS FOR POST-APPROVAL CONTROL AND MONITORING PURPOSES

Methods for post-approval control and monitoring purposes are reported in Volume 3 CA B.5.2 of this DAR.

B.5.3. REFERENCES RELIED ON

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KCP 5.1.1/1	Muenz J.	2017 a	Determination of Cinmethylin in EC formulations by means of GC 2017/1121786 Allessa GmbH, Frankfurt/Main, Germany Fed.Rep. no Unpublished	No	No	Not applicable	BASF	None
KCP 5.1.1/2	Nemitz A.	2015 a	Validation of the analytical method AFL0925/01: Determination of Cinmethylin in BAS 684 02 H by means of GC 2015/1043123 BASF SE, Limburgerhof, Germany Fed.Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None
KCP 5.1.1/3	Muenz J.	2017 b	Determination of Cinmethylin in EC formulations by means of GC 2017/1121789 BASF SE, Limburgerhof, Germany Fed.Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None
KCP 5.1.1/05	Bacher R	2017 a	Additional validation to the analytical method for the determination of the solvents Toluene and o-Xylene in EC-formulations containing Cinmethylin by means of Headspace GC for BAS 684 03 H 2017/1077862 yes Unpublished	No	Yes	Data for first approval	BASF	None
KCP 5.1.1/06	Tolle S	2016 a	Determination of the solvents Toluene and o-Xylene in EC formulations containing Cinmethylin by means of Headspace GC 2016/1296122	No	No	Not applicable	BASF	None

			No Unpublished					
KCP 5.1.1/07	Bacher R	2017 b	Validation of an analytical method for the determination of the solvents Toluene and o-Xylene in EC formulations containing Cinmethylin by means of Headspace GC 2016/1296123 yes Unpublished	No	Yes	Data for first approval	BASF	None