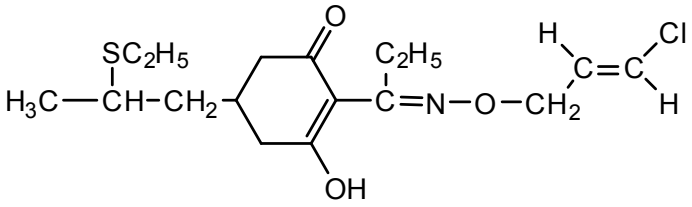
SYRICIT

Clethodim



CIPAC Collaborative Trial
CIPAC 5397/R, full scale study

Hi m

Technical Material and Formulated Products

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1. List of Participants

After the full scale collaborative trial of clethodim was initiated by CIPAC, we received 13 international laboratory applications for participating in the collaborative study.

The clethodim samples were distuibuted to the participants. Unfortunately, the samples to Currenta GmbH & Co. OHG Germany were partly damaged because of bottle breakage. The results were not returned from PT Agriculture Construction Indonesia. So the results from 11 laboratories were used for statistics.

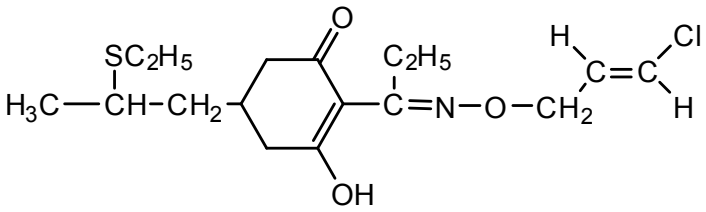
The all participants were listed below.

NAME	ORGANIZATION	COUNTRY
Dr. Christian Mink	Syngenta Crop Protection AG	Switzerland
Judy Dong	Shandong Binnong Technology Co., Ltd.	China

Peize Li	Institute for the Control of Agrochemicals, MOA	China
Mirror	Shanghai Xiaoming Testing Technology Service Co., Ltd	China
Meiqin Zhao	Zhejiang Tianfeng Bioscience Co., Ltd.	China
Ping Wang	Beijing Qincheng Yixin Technology Development Co., Ltd	China
Rachel Joseph	Jiangsu Rotam Chemistry Co., Ltd	China
Xianmei Meng	Shenyang Sciencreat Chemicals Co., LTD	China
Yang Guangshan	Wuwei Lianshuo Biotechnology Co., Ltd.	China
Weiwei Liu	Hebei Lansheng Biotechnology Co., Ltd	China
Hongfeng Sun	Shenyang SYRICI Testing Co., Ltd.	China
Agus Salim	PT Agriculture Construction (AGRICON)	Indonesia
Dr. Michael Haustein	Currenta GmbH & Co. OHG	Germany

2. General Information

Clethodim



ISO Common name Clethodim

Chemical name

(5RS)-2-[(1EZ)-N-{[(2E)-3-chloroallyl]oxy} propanimidoyl]-5-[(2RS)-2-(ethylthio)propyl]-3-hydroxycyclohex-2-en-1-one(IUPAC)

2-[1-[[[(2E)-3-chloro-2-propen-1-yl]oxy]imino]propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one (CA, 99129-21-2)

Empirical formula	$C_{17}H_{26}ClNO_3S$
RMM	359.9
m.p.	Decomposition
v.p.	＜0.01 mPa at 20°C
Solubility	Soluble in most solvents
Stability	Aqueous hydrolysis DT50 28 d (pH 5), 300 d (pH 7), 310 d (pH 9). Aqueous photolytic DT50 (sterile buffers, pH 5, 7 and 9), 1.7-9.6 d (without photosensitiser), 0.5-1.2 d (with photosensitiser).
Description	The pure material is clear, amber liquid.
Formulation	Emulsifiable concentrates (EC)

3. Distribution of Samples

The following samples were provided to the partcipants:

Clethodim lithium reference substance 1 g
Lot No. 20231201, purity: 974 g/kg

Clethodim technical (TC1) 50 g
Batch No. 2024010701, approx. 950 g/kg

Clethodim technical (TC2) 50 g
Batch No. 2024010702, approx. 950 g/kg

Clethodim 37% technical concentrates (TK1) 50 g
Batch No. 2024010901, approx. 370 g/kg

Clethodim 37% technical concentrates (TK2) 50 g
Batch No. 2024011001, approx. 370 g/kg

Clethodim 240 g/L Emulsifiable concentrates (EC1) 60 mL
Batch No. 20240112, approx. 240 g/L

Clethodim 240 g/L Emulsifiable concentrates (EC2) 60 mL
Batch No. 20240113, approx. 240 g/L

Clethodim 120 g/L Emulsifiable concentrates (EC3) 60 mL
Batch No. 20240114, approx. 120 g/L

Clethodim 120 g/L Emulsifiable concentrates (EC4) 60 mL
Batch No. 20240115, approx. 120 g/L

4. Procedure

4.1. Outline of Method

Clethodim in the test substance is determined by HPLC method with a normal phase silica gel column and UV-detection at 254 nm. The analyte solution contains about 50 mg of Clethodim in 50 mL solution.

4.2. Program of Work

We requested the collaborators to:

1) conduct duplicate determinations on two different days for each of the eight samples;

2) inject each sample solution in duplicate and calculate the mean value;

3) check equilibration of the system before the determination;

4) describe operating conditions in detail;

5) attach the typical chromatograms for the eight samples.

5. Analytical Methods

5.1. Analytical Conditions

Lab	Liquid chromatograph integrator	Column	Mobile phase	Flow rate (mL/min)	Column temp(°C)
Proposed Conditions		Agilent Zorbax RX-SIL, 250×4.6 mm, 5μm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	room temperature
1	/	Agilent Zorbax RX-SIL 250x4.6mm, 5μm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	room temperature
2	Waters Corporation, e2695	RX-SIL 250x4.6mm, 5μm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	30
3	waters 2695/2996	Agilent Zorbax RX-SIL 250x4.6mm, 5μm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	30
4	Agilent, 1260 Infinity II	DICP Amylose (ATPC) 250x4.6mm, 5μm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	30

5	Agilent 1260,Infinity IIAltus	Phenomenex BONDCLONE 10 SILICA 300x3.90mm, 5 µm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	30
6	Waters 2695	Dikma Platisil Silica 250x4.6mm, 5µm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.0	room temperature
7	Shimadzu HPLC-PDA	Agilent Zorbax RX-SIL 250x4.6mm, 5µm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	35
8	Thermo Dionnex U3000	Agilent Zorbax RX-SIL 250x4.6mm, 5µm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	30
9	SHIMADZU LC-20AT SPD-20A	Inertsil SIL-100A 150x4.6mm, 5µm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	room temperature
10	Waters 2998PDA	Agilent Zorbax RX-SIL 250x4.6mm, 5µm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	room temperature
11	Agilent 1260,Infinity II	Agilent Zorbax RX-SIL 250x4.6mm, 5µm	n-hexane + ethyl acetate + acetic acid , 940 + 40 + 20 (v/v)	1.2	room temperature

5.2. Deviations from the Analytical Method

Lab 1: No deviations.

Lab 2: No deviations.

Lab 3: No deviations.

Lab 4: No deviations.

Lab 5: The column was Phenomenex BONDCLONE 10 SILICA 300x3.9mm, 5µm instead of the recommended 250x4.6mm, 5µm.

Lab 6: Flow rate was changed to 1.0 ml/min.

Lab 7: No deviations.

Lab 8: No deviations.

Lab 9: The column was Inertsil SIL-100A 150x4.6mm, 5µm.

Lab 10: No deviations.

Lab 11: No deviations.

5.3. Remarks about the Analytical Method

Lab 1: Repetition of Sample 2024010901 (Clethodim TK-1a1 + Clethodim TK-1a2).

Lab 2: No remarks.

Lab 3: No remarks.

Lab 4: No remarks.

Lab 5: No remarks.

Lab 6: No remarks.

Lab 7: No remarks.

Lab 8: The reference substance showed some difficulty to dissolve, sometimes it formed crystalline particles and not easy to dissolve completely in the solvent. When we added 0.6 ml acid and 5ml mobile phase, we noticed that some crystalline particles are formed if we do not shake it immediately and followed by sonication. We shaked vigorously for 2 mins and sonicated for 2 mins. after making up to volume we sonicated again. Only at the final sonication, we observed completely dissolution. if other labs have observed the same situation, it is recommended to keep a note in the CIPAC method.

Lab 9: No remarks.

Lab 10: Analysis performed well.

Lab 11: I worked in UPLC, I adapted the sample solution with the additional dilution. No problems encountered.

6. Statistical Evaluation

Samples were sent to 13 laboratories. 11 of them sent back results.

The statistical evaluation of the data was done following DIN ISO 5725 and “Guidelines for CIPAC Collaborative Study Procedure for Assessment of Performance of Analytical Methods”.

No outliers or stragglers were found in all labs.

7. Results

Table 1: Clethodim TC1 (Batch No: 2024010701)

Lab	Day 1		Day 2		Mean g/kg	Std. Dev.
	A	B	A	B		
1	967.1	963.4	966.8	964.4	965.4	1.80
2	952.7	953.4	947.0	952.2	951.3	2.92
3	970.4	974.2	970.3	967.7	970.6	2.68
4	950.3	953.3	951.7	953.3	952.1	1.46
5	962.3	957.5	966.5	958.8	961.3	4.03
6	956.4	952.6	954.4	954.5	954.4	1.53
7	959.4	957.3	958.3	954.7	957.4	2.01
8	969.6	971.5	970.6	975.4	971.8	2.55
9	962.6	970.5	966.8	964.4	962.6	3.40
10	959.2	961.1	960.2	962.3	960.7	1.31
11	961.9	962.7	951.9	959.9	959.1	4.97

No outliers or stragglers.

Fig.1: Clethodim TC1 (Batch No: 2024010701)
All labs (No outliers or stragglers were found.)

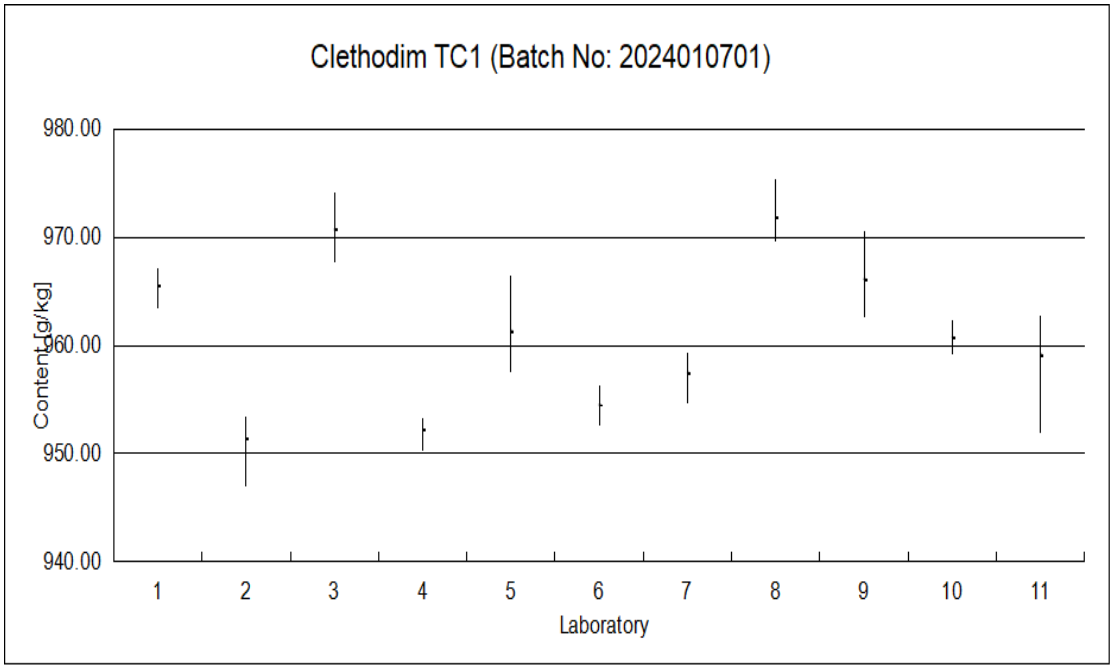


Table 2: Clethodim TC2 (Batch No: 2024010702)

Lab	Day 1		Day 2		Mean g/kg	Std. Dev.
	A	B	A	B		
1	965.4	966.6	966.0	968.7	966.7	1.43
2	955.3	956.8	949.8	954.2	954.0	3.02
3	969.5	969.4	968.7	971.6	969.8	1.25
4	953.0	956.4	951.0	949.5	952.5	3.01
5	964.7	967.5	959.5	964.0	963.9	3.30
6	949.4	953.3	952.4	948.0	950.8	2.51
7	959.2	958.2	955.1	953.9	956.6	2.53
8	960.0	957.2	956.6	955.5	957.3	1.92
9	961.7	967.0	962.4	960.8	963.0	2.77
10	959.3	953.3	956.9	959.1	957.1	2.77
11	954.8	946.6	944.7	943.3	947.3	5.16

No outliers or stragglers.

Fig.2: Clethodim TC2 (Batch No: 2024010702)
All labs (No outliers or stragglers were found.)

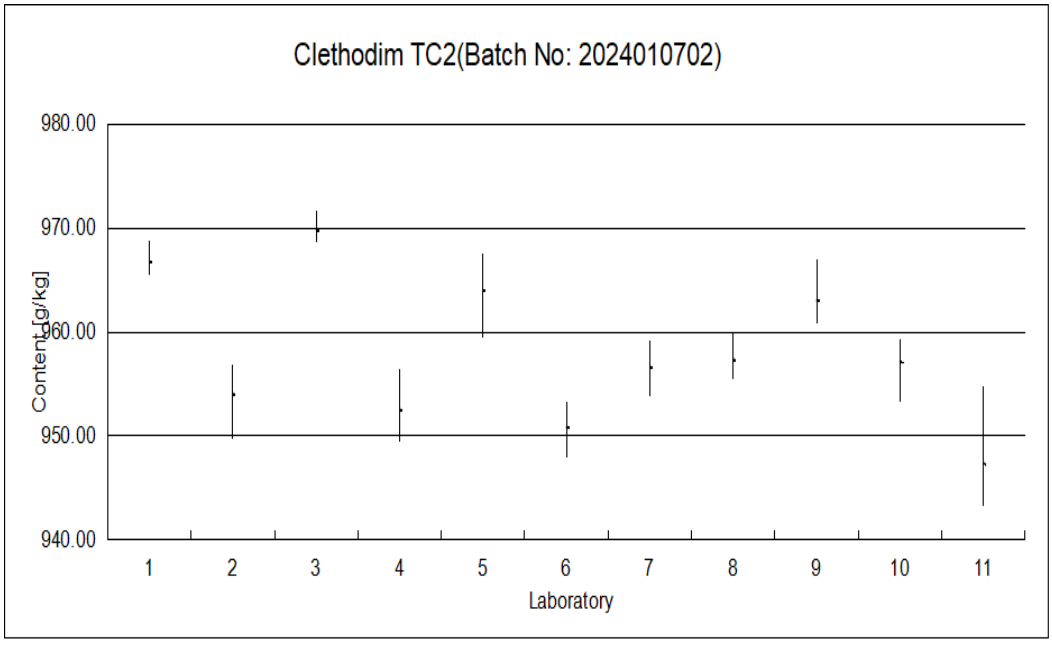


Table 3: Clethodim TK1 (Batch No: 2024010901)

Lab	Day 1		Day 2		Mean g/kg	Std. Dev.
	A	B	A	B		
1	385.7	383.2	384.9	386.1	385.0	1.28
2	379.8	379.3	377.8	375.6	378.1	1.88
3	369.7	370.6	369.5	372.3	370.5	1.28
4	375.5	374.7	373.3	371.6	373.8	1.69
5	384.6	383.2	384.1	382.6	383.6	0.93
6	377.7	379.2	383.5	384.0	381.1	3.16
7	381.5	379.0	375.8	374.5	377.7	3.17
8	375.0	374.3	377.6	379.8	376.7	2.53
9	383.4	384.8	384.3	385.4	384.5	0.85
10	382.0	383.4	380.2	379.3	381.2	1.82
11	376.0	373.8	378.2	380.2	377.1	2.75

No outliers or stragglers.

Fig.3: Clethodim TK1 (Batch No: 2024010901)
All labs (No outliers or stragglers were found.)

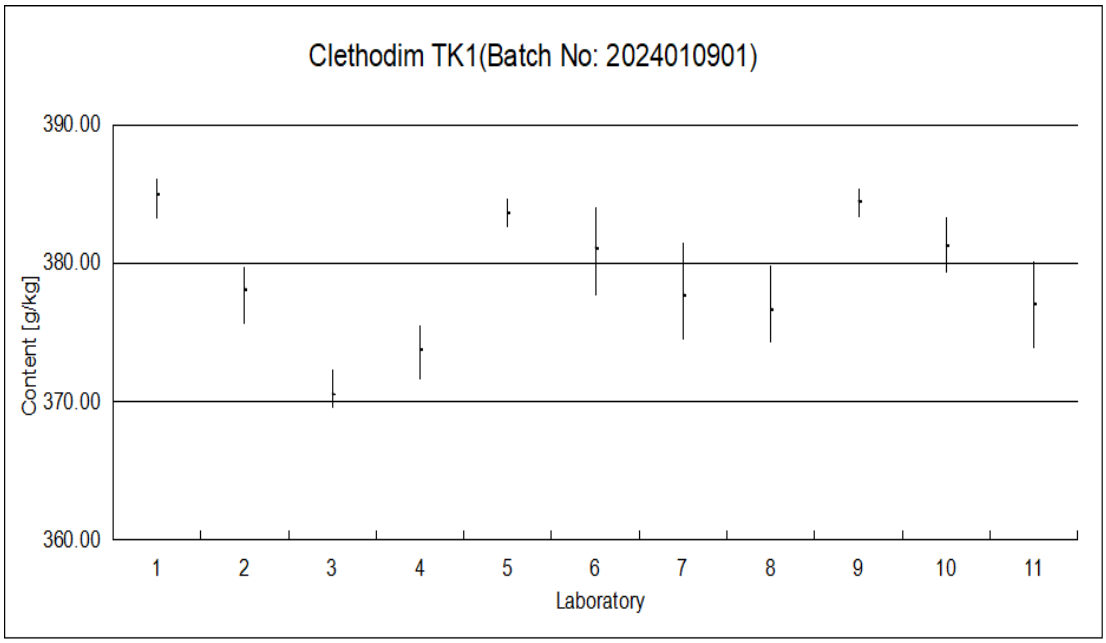


Table 4: Clethodim TK2 (Batch No: 2024011001)

Lab	Day 1		Day 2		Mean g/kg	Std. Dev.
	A	B	A	B		
1	383.4	383.9	383.0	381.0	382.8	1.25
2	379.1	384.5	374.3	373.7	377.9	5.04
3	372.2	374.8	374.4	374.0	373.9	1.15
4	373.4	375.8	371.7	373.4	373.6	1.68
5	377.3	382.4	381.1	382.3	380.8	2.39
6	381.2	379.6	382.4	378.1	380.3	1.86
7	374.3	377.2	373.2	373.9	374.7	1.74
8	374.1	376.9	379.1	375.2	376.3	2.17
9	384.3	385.1	385.7	386.6	385.4	0.97
10	382.2	384.5	377.8	374.9	379.8	4.33
11	374.6	370.9	375.3	376.5	374.3	2.40

No outliers or stragglers.

Fig.4: Clethodim TK2 (Batch No: 2024011001)
All labs (No outliers or stragglers were found.)

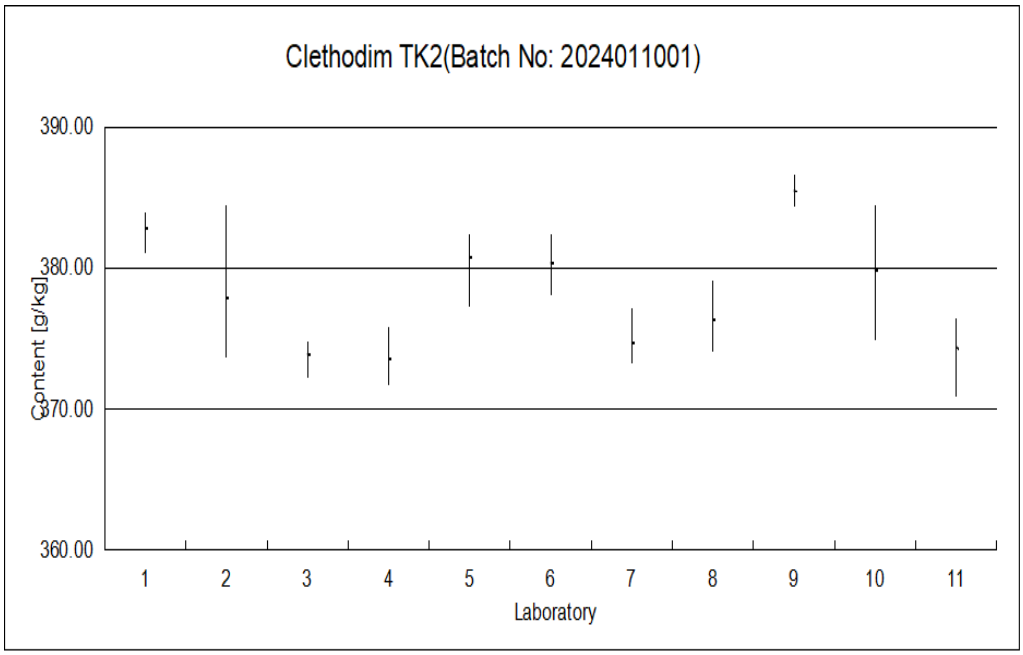


Table 5: Clethodim EC1 (Batch No: 20240112)

Lab	Day 1		Day 2		Mean g/kg	Std. Dev.
	A	B	A	B		
1	252.7	252.3	252.9	252.7	252.7	0.25
2	252.6	253.0	247.8	246.8	250.1	3.22
3	251.8	252.9	249.7	251.0	251.4	1.35
4	252.5	252.0	249.9	249.9	251.1	1.37
5	252.6	252.1	254.0	252.3	252.7	0.85
6	249.5	249.9	249.3	252.4	250.3	1.43
7	252.2	249.9	253.8	250.2	251.5	1.82
8	247.8	253.5	251.8	252.9	251.5	2.55
9	253.2	252.9	253.2	253.2	253.1	0.14
10	252.2	253.0	249.2	251.1	251.4	1.63
11	245.6	243.0	249.8	247.8	246.5	2.93

No outliers or stragglers.

Fig.5: Clethodim EC1 (Batch No: 20240112)
All labs (No outliers or stragglers were found.)

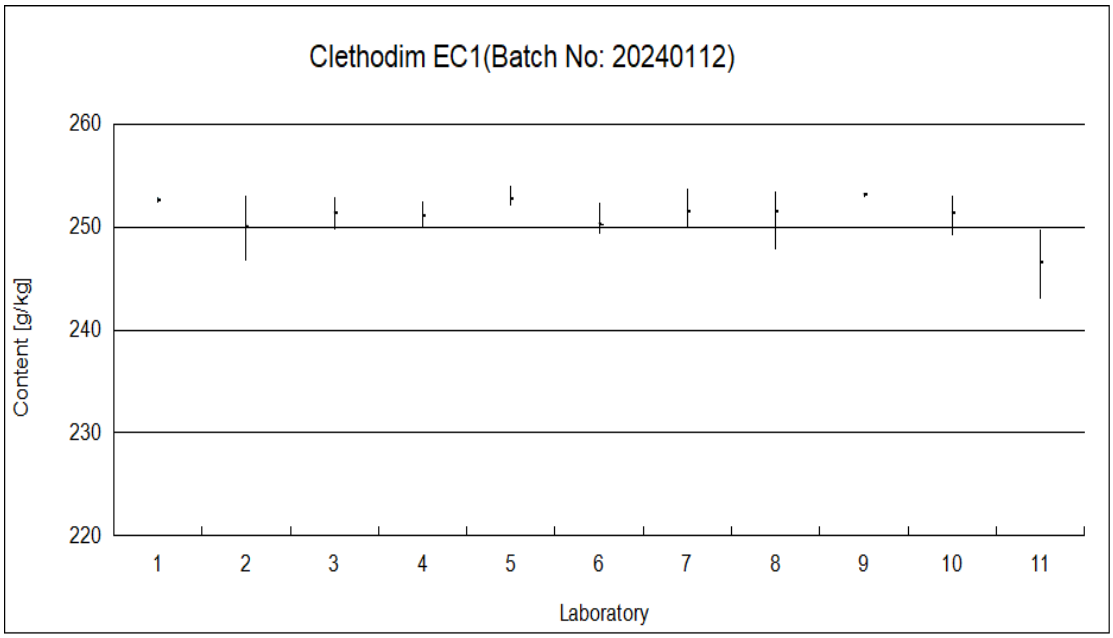


Table 6: Clethodim EC2(Batch No: 20240113)

Lab	Day 1		Day 2		Mean g/kg	Std. Dev.
	A	B	A	B		
1	252.3	251.1	251.7	252.5	251.9	0.62
2	249.6	254.3	250.2	248.3	250.6	2.61
3	249.5	250.8	247.6	248.0	249.0	1.47
4	250.0	250.9	248.7	250.5	250.0	0.99
5	250.2	251.4	250.8	252.3	251.2	0.88
6	249.2	252.2	251.9	248.4	250.4	1.92
7	249.7	249.6	249.2	251.9	250.1	1.23
8	253.3	248.9	254.3	254.4	252.7	2.61
9	252.4	253.9	253.6	252.8	253.2	0.67
10	252.4	254.8	252.3	251.9	252.9	1.33
11	242.3	241.8	247.9	245.7	244.4	2.90

No outliers or stragglers.

Fig.6: Clethodim EC2 (Batch No: 20240113)
All labs (No outliers or stragglers were found.)

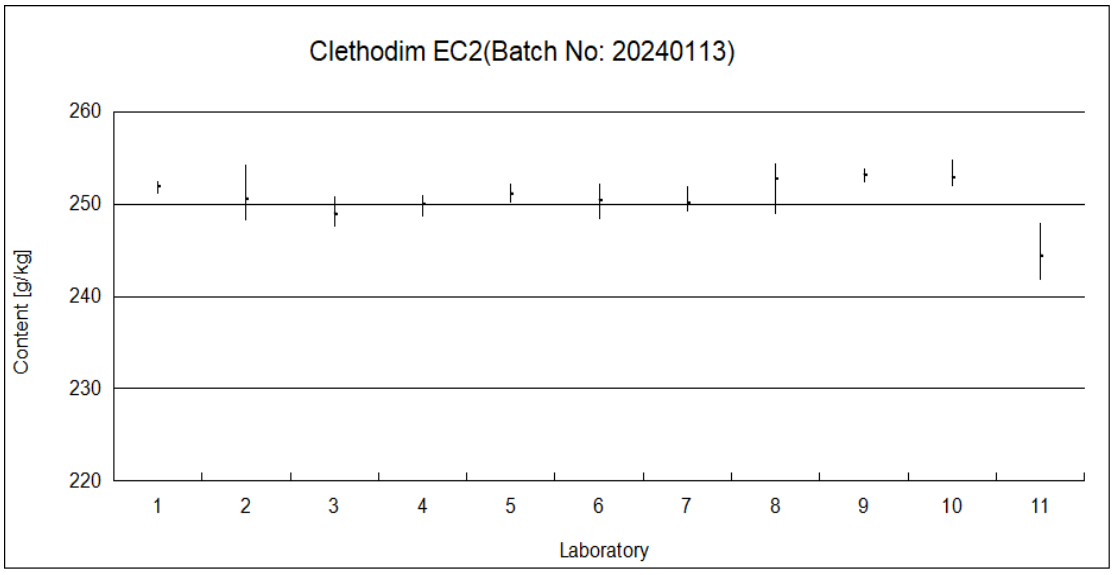


Table 7: Clethodim EC3 (Batch No: 20240114)

Lab	Day 1		Day 2		Mean g/kg	Std. Dev.
	A	B	A	B		
1	133.0	130.8	132.2	131.7	131.9	0.92
2	133.2	132.6	130.8	131.3	132.0	1.14
3	130.2	130.0	130.0	130.4	130.2	0.19
4	131.9	132.0	132.4	132.9	132.3	0.46
5	133.3	133.4	133.2	133.6	133.4	0.18
6	131.9	132.2	132.8	132.1	132.2	0.37
7	132.0	131.9	132.9	130.9	131.9	0.81
8	133.0	133.2	133.0	133.4	133.1	0.19
9	129.1	129.7	129.3	128.9	129.2	0.35
10	132.1	133.6	132.6	133.3	132.9	0.66
11	127.3	127.1	129.9	142.3	131.6	7.21

No outliers or stragglers.

Fig.7: Clethodim EC3 (Batch No: 20240114)
All labs (No outliers or stragglers were found.)

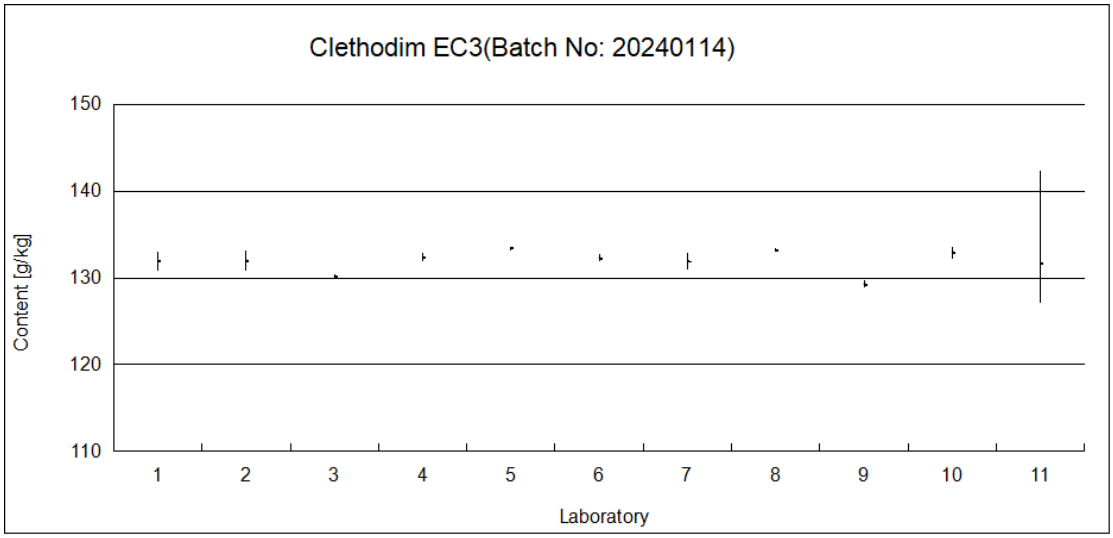
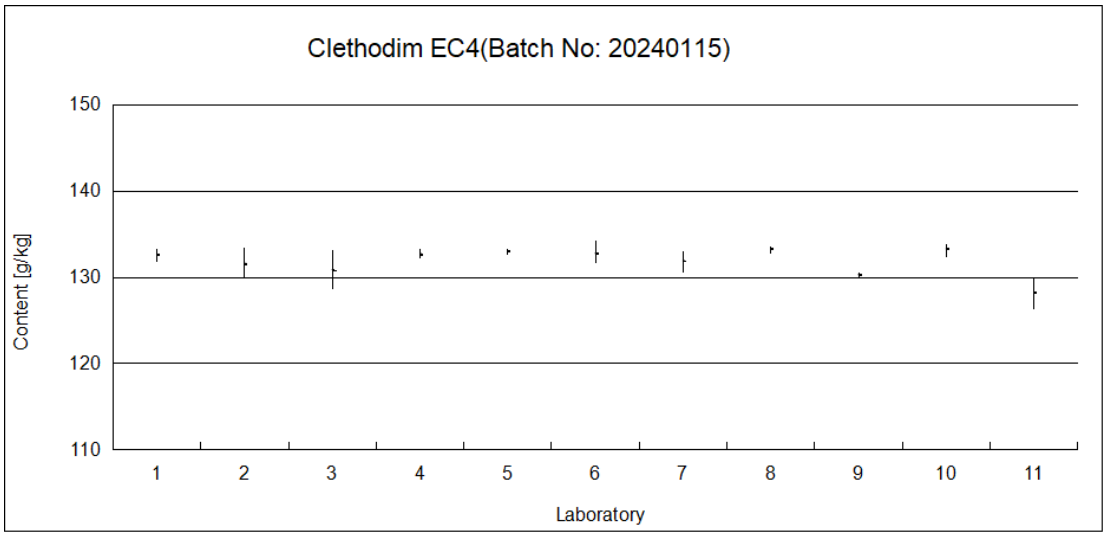


Table 8: Clethodim EC4 (Batch No: 20240115)

Lab	Day 1		Day 2		Mean g/kg	Std. Dev.
	A	B	A	B		
1	133.4	132.2	132.9	131.7	132.5	0.72
2	132.5	133.5	129.9	130.4	131.6	1.70
3	129.6	128.6	131.9	133.2	130.8	2.10
4	132.8	132.4	132.2	133.4	132.7	0.53
5	132.6	133.1	133.1	133.3	133.0	0.28
6	134.2	131.6	131.9	133.1	132.7	1.21
7	133.1	131.3	132.5	130.6	131.9	1.14
8	133.6	132.8	133.4	133.2	133.2	0.36
9	130.5	130.2	130.2	130.1	130.2	0.18
10	133.2	133.6	132.4	133.8	133.3	0.64
11	127.2	126.4	129.4	130.0	128.2	1.74

No outliers or stragglers.

Fig.8: Clethodim EC4 (Batch No: 20240115)
All labs (No outliers or stragglers were found.)



8. Summary of the results

Table 9 Summary of the results of all laboratories

	TC1	TC2	TK1	TK2	EC1	EC2	EC3	EC4
x	960.9	959.2	379.0	377.7	251.4	250.4	132.0	132.2
L	11	11	11	11	11	11	11	11
S_r	2.83	2.88	2.10	2.59	1.86	1.75	2.25	1.15
S_R	7.39	7.43	4.90	4.57	2.41	2.87	2.31	1.84
r	8.01	8.14	5.94	7.32	5.25	4.96	6.38	3.25
R	20.91	21.04	13.87	12.95	6.82	8.13	6.54	5.21
RSD_r	0.29	0.30	0.55	0.68	0.74	0.70	1.71	0.87
RSD_R	0.77	0.78	1.29	1.21	0.96	1.15	1.75	1.39
$RSD_{R(Hor)}$	2.01	2.01	2.31	2.32	2.46	2.46	2.71	2.71
HorRat	0.38	0.39	0.56	0.52	0.39	0.47	0.65	0.51

(values given in units of g/kg)

Where:

x = average, in unit of g/kg
L = number of laboratories
S_r = repeatability standard deviation
S_R = reproducibility standard deviation $= \sqrt{(S_r^2 + S_L^2)}$
r = repeatability ($S_r \cdot 2.8$)
R = reproducibility ($S_R \cdot 2.8$)
RSD_r = repeatability relative standard deviation ($100 \cdot S_r/x$)
RSD_R = reproducibility relative standard deviation ($100 \cdot S_R/x$)
$RSD_R(Hor)$ = Horwitz value calculated from: $2^{(1-0.5\log c)}$
where c = the concentration of the analyte as a decimal fraction

9. Statistical formulas

Yi = mean of the various laboratories
Si = standard deviation
P = number of laboratories
n = number of measurements (here n=4)

$$T_1 = \sum_{i=1}^{p} Yi$$

$$T_2 = \sum_{i=1}^{p} Yi^2$$

$$T_3 = \sum_{i=1}^{p} Si^2$$

Repeatability and reproducibility were calculated as follows:

$$S_r^2 = \frac{T_3}{P}$$

$$S_L^2 = \frac{PT_2 - T_1^2}{P(P-1)} - \frac{S_r^2}{n}$$

$$S_R^2 = S_r^2 + S_L^2$$

$$r = 2.8 * \sqrt{S_r^2}$$

$$R = 2.8 * \sqrt{S_R^2}$$

10. Discussion

Following the successful outcome of the small scale collaborative study organized by SYRICIT, an international CIPAC collaborative study was initiated in March 2024 to test a specific HPLC method for the determination of Clethodim.

13 laboratories had announced to participate the CIPAC trial and 11 of them sent back results.

The data from each of the laboratories were reviewed to determine if there were any problems with analysis procedure, chromatography or reporting results, which might affect the analyses results. The changes, deviations, and observations which were noted will not be expected to affect the analyses results significantly.

There were no stragglers and outliers for all the eight samples according to Cochran test and Grubbs test, and the results of 11 laboratories participated in the collaborative trial were taken into account for the statistical evaluation, the Horwitz criteria were fulfilled for all the eight samples TC1, TC2, TK1, TK2, EC1, EC2, EC3 and EC4.

Conclusion:

We would like to propose the analytical method for Clethodim to become provisional.

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