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AMBIENTE
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ISTITUTO SUPERIORE DI SANITÀ

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Dipartimento Ambiente e Salute

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2019, v, 38 p. Rapporti ISTISAN 19/21

In 2018 the second Proficiency Test (PT) was organized among laboratories all over Europe on plant protection products available on the Italian market. The aim of the trial was to find out the quantity of active ingredient on the different formulation of the plant protection products. Ten Italian laboratories and sixteen ones from the rest of European Union, who routinely deal with pesticides, were invited to participate. Laboratories are not obligated to take part in the PT; by the way, all the participants sent their results. All laboratories obtained data with acceptable values of z-score within the limits, except for three of them who got higher than -3.5 z-score value for the active substances Amisulbrom, one higher than +3.5 z-score value for Dimethomorph and Propiconazole and two for Pirimiphos-Methyl. All the laboratories enjoyed taking part at this trial so another one is planned for the 2020.

Key words: Proficiency test; Plant protection products; Amisulbrom; Dimethomorph; Pirimiphos-Methyl; Propiconazole.

Istituto Superiore di Sanità
Risultati del primo esercizio interlaboratorio sui prodotti fitosanitari nel 2019.
Angela Santilio, Chiara Pompili, Roberto Cammarata, Arianna Giambenedetti
2019, v, 38 p. Rapporti ISTISAN 19/21 (in inglese)

Nel 2018 è stato organizzato il secondo esercizio interlaboratorio su prodotti fitosanitari disponibili sul mercato nazionale. L'esercizio riguardava la determinazione del contenuto di principio attivo presente in prodotti fitosanitari di diversa formulazione. Sono stati invitati a partecipare 10 laboratori italiani preposti al controllo dei prodotti fitosanitari e 16 laboratori comunitari interessati ai controlli sui prodotti fitosanitari. La partecipazione è su base volontaria e hanno aderito tutti i partecipanti. Tutti i laboratori italiani e europei hanno ottenuto risultati con valori di z-score entro i limiti definiti ad eccezione di 3 laboratori che hanno ottenuto valori di z-score > -3,5 per la sostanza Amisulbrom; un solo laboratorio ha ottenuto un valore di z-score > +3,5 nell'analisi di Dimethomorph e Propiconazole e due per il Pirimiphos-Methyl. L'esercizio è stato accettato con entusiasmo da parte dei laboratori ed è in progetto l'organizzazione di un secondo esercizio interlaboratorio per il 2020.

Parole chiave: Esercizio interlaboratorio; Prodotti fitosanitari; Amisulbrom; Dimethomorph; Pirimiphos-Methyl; Propiconazole

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ABBREVIATIONS

AFSCA	Agence fédérale pour la sécurité de la chaîne alimentaire (Federal Agency for the Safety of the Food Chain)
AAPCO	Association of American Pesticide Control Officials
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council
CV	Coefficient of Variation
EC	Emulsifiable Concentrate
GC	Gas Chromatography
GR	Granules
ISO	International Organization for Standardization
ITPT	Italian Proficiency Test
L	Liquid
LC	Liquid Chromatography
MAD	Median Absolute Deviation
MS	Mass Spectrometry
N/A	Not Available
PDA	PhotoDiode Array
PPP	Plant Protection Product
PPP01	Plant Protection Product number 1
PPP02	Plant Protection Product number 2
PPP03	Plant Protection Product number 3
PPP04	Plant Protection Product number 4
PT	Proficiency Test
SD	Standard Deviation
UV	UltraViolet
VWD	Variable Wavelength Detector
WG	Wettable dispersible Granules
WP	Wettable Powder
z-score	Standard Score

Symbols

σ_P	standard deviation for proficiency test
T-test	statistic test of Student's t distribution

PREFACE

The European legislation – Regulation (EC) 1107/2009 – on Plant Protection Products (PPPs) regulates the authorisation, placing on the market, use and control of PPPs and of any active substances, safeners, synergists, co-formulants and adjuvants, which they might contain or of which they might consist. The objective of those rules is to ensure a high level of protection of both human and animal health and of the environment through evaluation of the risks posed by PPPs, while improving the functioning of the Union market through harmonisation of the rules for their placing on the market and while also improving agricultural production.

In addition, the Regulation (EU) 2017/625 establish a harmonised European Union framework for the organisation of official controls and official activities taking into account the rules on official controls laid down in Regulation (EC) 882/2004 and in relevant sectoral legislation, and the experience gained from the application of those rules.

The laboratories designated by the competent authorities to perform analyses on PPP samples taken in the context of official controls should possess the expertise, equipment, infrastructure and staff to carry out such tasks to the highest standards. To ensure sound and reliable results, those laboratories should be accredited for the use of these methods according to standard EN ISO/IEC 17025.

One of the instrument to reach a high quality standard and performance is the participation to the interlaboratory test (Proficiency Test, PT) to demonstrate that the analytical data obtained from laboratories are reliable.

In the area of PPPs there are two organizations that plan PTs:

– Association of American Pesticide Control Officials (AAPCO)
  an international organization that schedules PT on the active ingredient content on PPP on the basis of the American monitoring programmes.

– Agence fédérale pour la sécurité de la chaîne alimentaire (AFSCA)
  a European organization that plans PT on physical chemical properties for PPPs.

On the basis of this information, it is important to organize PTs for the active ingredient content for the national official laboratories. This activity was planned in the framework of the collaboration with Health Ministry and the Istituto Superiore di Sanità (ISS, the National Institute of Health in Italy). Due to the national monitoring programs are in compliance with the European monitoring programs it is useful to enlarge the invitation to European Member State laboratories that work on this issues.

INTRODUCTION

In January 2019, all relevant Italian laboratories and European Member State laboratories were invited to participate in the 2nd Italian PT on PPPs (later indicated as ITPT2019).

The announcement letter (Appendix A) was sent to the laboratories on 15th January, according to the calendar the laboratories was asked to forward the invitation. The invitation was send to 10 Italian laboratories and to 16 European laboratories. All laboratories agreed to participate in the test.

For the PT four different commercial products containing three active ingredients (Amisulbrom 5%, Dimethomorph 6%, Pirimiphos-Methyl 5%, Propiconazole 25%) were shipped to the laboratories.

1. PROFICIENCY TEST ON PLANT PROTECTION PRODUCTS

1.1. Test materials

The test materials of the ITPT2019 consisted of four PPPs obtained from manufacturer and available from Italian market.

The product types are: Wettable Dispersible Granules (WG), Wettable Powder (WP), Liquid (L), and an Emulsifiable Concentrate (EC) at a declared concentration reported in Table 1.

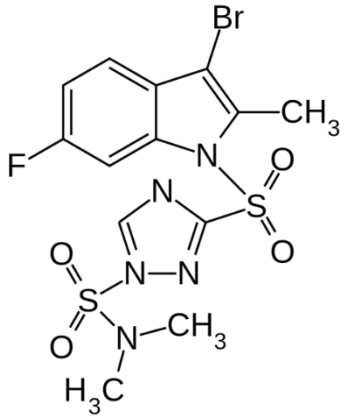
Table 1. Test materials of ITPT2019

Check Sample N.	Product description	Active ingredient	Declared level %
PPP01	Water dispersible granules	Amisulbrom	5
PPP02	Wettable powder	Dimethomorph	6
PPP03	Liquid	Pirimiphos-Methyl	5
PPP04	Emulsifiable concentrate	Propiconazole	25

For the preparation of the subsamples to send each laboratories, the PPs were mixed mechanically and shared in 26 samples for a total of 52 plastic containers and 52 glass bottles sealed and stored at ambient temperature before the shipment to the participants. Each laboratory received four samples. Nothing was added to our samples.

1.2. Description of the active substances in the PPPs

1.2.1. Amisulbrom



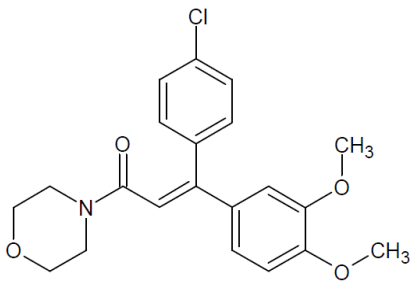
Common name
3-(3-Brom-6-fluor-2-methylindol-1-ylsulfonyl)-N,N- dimethyl-1H-1,2,4-triazol-1-sulfonamid

Structure Formula $C_{13}H_{13}BrFN_5O_4S_2$

CAS number 348635-87-0

The product has a molecular weight of 466.3 g/mol. On the market it is found as just Amisulbrom or with Mancozeb or Folpet, the one used for this PT was with Folpet. Amisulbrom belongs to the class of QiI (Quinone inside Inhibitors) Fungicides. It is often used on vine plants, potato and tomato. It is moderately toxic for mammal's animals.

1.2.2. Dimethomorph



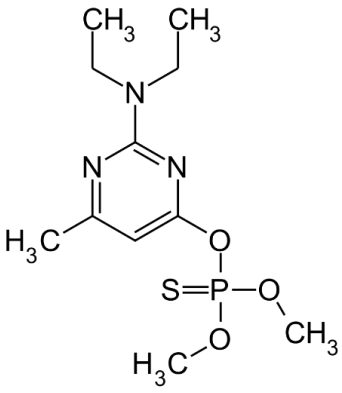
Common name
3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)-1-morpholin-4-ylprop-2-en-1-one

Structure formula $C_{21}H_{22}ClNO_4$

CAS number 110488-70-5

Dimethomorph is the common name for identify both the configuration but the Z- or E- isomers, but only the Z-isomer has a fungicidal activity. It has a molecular weight of 387.9 g/mol. Dimethomorph is used as a wood preservative to control downy mildew on vines, and to control late blight on tomatoes and potatoes. The EPA has classified dimethomorph as Toxicity Class III - slightly toxic.

1.2.3. Pirimiphos-Methyl



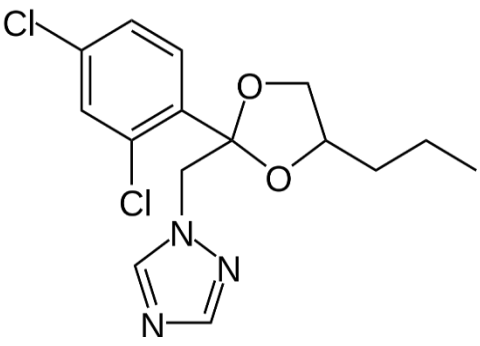
Common name
O-[2-(Diethylamino)-6-methylpyrimidin-4-yl] O,O-dimethyl phosphorothioate

Structure formula $C_{11}H_{20}N_3O_3PS$

CAS number 29232-93-7

Pirimiphos-methyl is an organophosphorus compound that is used in a wide range of pesticidal applications. This is one of several compounds used for vector control of *Triatoma*. These insects are implicated in the transmission of Chagas disease in the Americas. It has a molecular weight of 305.3 g/mol.

1.2.4. Propiconazole



Common name
1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1,2,4-triazole

Structure formula $C_{15}H_{17}Cl_2N_3O_2$

CAS number 60207-90-1

Propiconazole is a triazole fungicide, also known as a DMI, or demethylation inhibiting fungicide due to its binding with and inhibiting a precursor to ergosterol. Is a mixture of four stereoisomers and it has a molecular weight of 342.22 g/mol. Propiconazole is used agriculturally as a systemic fungicide on turfgrasses grown for seed and aesthetic or athletic value. It is also used in combinationth permethrin in formulations of wood preserver.

1.3. Homogeneity and stability test

Homogeneity and stability tests were performed according to the ISO 13528:2015(E) - Annex B and the International Harmonized Protocol.

1.3.1. Homogeneity

Regarding the homogeneity test, ten bottles were randomly chosen and analysed in duplicate in two different days.

Considering that the σ_{PT} is unknown, the statistical significant differences between PT items used was evaluated with the analysis of variance T-test at α=0.05, if the data series are more than two will need the Fisher Test. The T-test shows a significativity level (P) higher than 0.05 for each active substance. It is possible to say the samples are not different one each other: they are homogeneous.

The results are shows in the Table 2 for all compounds.

Table 2. Homogeneity results of the PT samples

Sample ID	Amisulbrom		Dimethomorph		Pirimiphos-Methyl		Propiconazole	
	a	b	a	b	a	b	a	b
#1	5.23	5.24	6.48	6.58	5.02	5.19	25.5	24.3
#2	5.19	5.23	6.66	6.59	5.03	5.18	23.2	22.2
#3	5.12	5.22	6.52	6.39	5.11	5.60	22.2	23.5
#4	5.24	5.22	6.60	6.52	4.95	5.02	23.3	23.9
#5	5.18	5.24	6.48	6.49	5.23	5.49	24.6	24.5
#6	5.18	5.17	6.53	6.41	5.38	5.16	25.1	24.8
#7	5.27	5.14	6.44	6.55	5.31	5.43	23.6	24.9
#8	5.27	5.06	6.40	6.40	5.00	5.08	24.8	25.1
#9	5.14	5.23	6.30	6.43	4.91	5.09	25.2	24.8
#10	5.24	5.24	6.57	6.60	5.13	5.12	24.8	25.4
Mean	5.20		6.50		5.17		24.3	
SD	0.055		0.092		0.186		0.994	
t**	0.281		0.046		1.618		0.26	
P***	0.782		0.963		0.123		0.798	
Homogeneity	YES		YES		YES		YES	

a, b: replicates of the same sample
t**: T of Student Test
P***: significativity level; SD: Standard Deviation

1.3.2. Stability

The stability test was performed using two bottles, randomly chosen, which were analysed in duplicate in two occasions and each occasion twice:

- Day 1: before the shipment of the samples between November and December 2019;
- Day 2: at the deadline for reporting results on June 2019.

Stability test was judged acceptable as the percentage difference of concentration, for each active substance was found less than 10%. As presented in Table 3, there was a slight decrease in the pesticide concentration of Pirimiphos-Methyl showed during the PT, but still acceptable.

Table 3. Summary of stability data (ITPT2019)

Active ingredient	Analysis Nov/Dec	Analysis June	Declared Level %
Amisulbrom	5.24	4.97	5
Dimethomorph	6.25	6.26	6
Pirimiphos-Methyl	5.17	4.02	5
Propiconazole	23.0	24.9	25

Tables 4, 5, 6 and 7 show the individual results for each substance. The deviation calculated with reference to the 1st analysis and to the declared label show a deviation less than 10% for all substances. The products can be considered stable.

Table 4. AMISULBROM: results of stability test (ITPT2019)

Parameter	November/December				June			
	Replicate 1		Replicate 2		Replicate 1		Replicate 2	
	inj 1	inj 2	inj 1	inj 2	inj 1	inj 2	inj 1	inj 2
Sample 1	5.03	5.03	5.53	5.56	4.57	4.59	5.64	5.64
Sample 2	5.29	5.28	5.1	5.07	4.58	4.58	5.1	5.08
Mean	5.16		5.32		4.58		5.365	
SD	0.147		0.266		0.008		0.318	
Mean of 2 days	5.24				4.97			
Standard Deviation of 2 days	0.207				0.163			
Deviation (ref 1st Analysis %)/ [(M2-M1)/M1]*100	3.054							
Deviation (ref to declared label %)/ [(SM-20)/20]*100	2.088							
Stability Mean	5.10		Declared Label		5.00			
Stability Standard Deviation	0.185		CV %		3.621			

Table 5. DIMETHOMORPH: results of stability test (ITPT2019)

Parameter	November/December				June			
	Replicate 1		Replicate 2		Replicate 1		Replicate 2	
	inj 1	inj 2	inj 1	inj 2	inj 1	inj 2	inj 1	inj 2
Sample 1	6.35	6.3	5.84	5.86	6.23	6.14	6.33	6.15
Sample 2	6.42	6.4	6.43	6.43	6.29	6.56	6.26	6.09
Mean	6.37		6.14		6.31		6.21	
SD	0.054		0.335		0.181		0.108	
Mean of 2 days	6.25				6.26			
Standard Deviation of 2 days	0.194				0.144			
Deviation (ref 1st Analysis %)/ [(M2-M1)/M1]*100	-3.57							
Deviation (ref to declared label %)/ [(SM-20)/20]*100	4.25							
Stability Mean	6.26		Declared Label		6.00			
Stability Standard Deviation	0.169		CV %		2.71			

Table 6. PIRIMIPHOS-METHYL: results of stability test (ITPT2019)

Parameter	November/December				June			
	Replicate 1		Replicate 2		Replicate 1		Replicate 2	
	inj 1	inj 2	inj 1	inj 2	inj 1	inj 2	inj 1	inj 2
Sample 1	4.92	5.21	5.56	5.2	3.67	4.1	4.26	3.54
Sample 2	5.04	4.9	5.07	5.44	3.60		4.60	4.18
Mean	5.02		5.32		3.885		4.15	
SD	0.142		0.223		0.271		0.443	
Mean of 2 days	5.17				4.02			
Standard Deviation of 2 days	0.183				0.357			
Deviation (ref 1st Analysis %)/ [(M2-M1)/M1]*100	5.98							
Deviation (ref to declared label %)/ [(SM-20)/20]*100	-8.175							
Stability Mean	4.59		Declared Label		5			
Stability Standard Deviation	0.123		CV %		2.68			

Table 7. PROPICONAZOLE: results of stability test (ITPT2019)

Parameter	November/December				June			
	Replicate 1		Replicate 2		Replicate 1		Replicate 2	
	inj 1	inj 2	inj 1	inj 2	inj 1	inj 2	inj 1	inj 2
Sample 1	23.4	23.5	23.3	23.2	22.2	21.6	27.0	26.6
Sample 2	23.2	22.3	22.7	22.5	25.3	25.4	25.3	25.6
Mean	23.10		22.93		23.63		5.30	
SD	0.548		0.386		2.007		0.806	
Mean of 2 days	23.01				24.88			
Standard Deviation of 2 days	0.467				1.406			
Deviation (ref 1st Analysis %)/ [(M2-M1)/M1]*100	-0.758							
Deviation (ref to declared label %)/ [(SM-20)/20]*100	-4.225							
Stability Mean	23.94		Declared Label		25			
Stability Standard Deviation	0.937		CV %		3.912			

1.4. Distribution of the samples and instructions for the participants

Two plastic transparent containers with red cup were filled (one with WP product and another one with WG products) two glass bottles was filled with L and EC products.

Each sample was shipped to the participating laboratories at ambient temperature.

An information message was sent out by e-mail during shipment so that laboratories make their own arrangements for the reception of the package, and a protocol was sent by e-mail.

The participants (Appendix B) were asked:
- to inform on the safe recipient of the samples in their laboratories;
- to report results in the appropriate form and send them to the organizer by e-mail along with the details of methodology used.

The samples were sent to the participant on 15th January 2019.
The deadline for results was 30th of April 2019.
The final report was dispatched to all participant at the end of June 2019.

1.5. Statistical evaluation of results

This PT has been evaluated using the modified z-score parameter to rate the laboratory performance for each active substance according to AAPCO protocol.

The outliers were calculated using both the modified z-score and adopting Horwitz limits and Thompson correction limits.

1.5.1. Robust mean

The purpose of using a robust estimator for the mean was to cope with the possibility of outlying data points without having to remove them from the sample.

The robust mean estimator used was the median.

1.5.2. Robust estimate of standard deviation

The robust estimate of the standard deviation used was the MAD_E value.

To obtain the MAD_E, calculate Median Absolute Deviation (MAD) from the sample median:

$$MAD = median\ (|X_i - median\ (Xi)|_{i=1,2\ldots n})$$

Calculate MAD_E:

$$MAD_E = K \times MAD$$

For normally distributed data, K= 1.483:

$$MAD_E = 1.483 \times MAD$$

1.5.3. Calculation of modified z-scores

Modified z-scores (Zi) for each laboratory were calculated as:

$$Zi = 0.6745 \times {}^{(Xi\ -\ median)} / MAD$$

Z values falling outside the range of $-3.5 \leq Zi \leq 3.5$ were marked as outliers.

1.5.4. Presentation of data

Data is presented graphically in two ways:
- a scatter plot showing each participating laboratory's two-day mean value for each analyte along with the associated standard deviation. These plots also show the upper and lower Horwitz (Thompson) limits for the sample, as well as median ±2 MAD_E.
- a plot of modified z-scores.

2. ANALYSIS OF THE SUBSTANCES

Description and statistical evaluation of the results are presented for each compound separately.

2.1. Amisulbrom

Regarding the active substance Amisulbrom, 26 boxes were sent to all over Europe, in particular 10 to Italian's Laboratories and 16 to European Laboratories outside Italy. They have been received 23 participation results; the three Laboratories missing are all from Italy. All the laboratories used for the analysis an LC instrument: 22 of them with a UV Detector and 1 with a MS Detector. It is interesting to note that almost half of the laboratories choose to use an In-house method and the other half a CIPAC method and just two applied a manufacturer's method, as shown in Table 8. At the same time, all the methods gave appreciable data.

Table 8. AMISULBROM: methods applied for analysis (ITPT2019)

Laboratories	In-House	CIPAC	Manufacturer's
Number	12	9	2

A statistical evaluation based on a robust estimator (median) instead of the mean was applied on the collected data. The purpose of this choice was to cope the possibility of outlying data points without having to remove them, so it was used the median and the standard deviation.

Figure 1 shows the lab's values of modified Z-score. The results obtained are laudable data, most of them are inside the modified z-score range of $-3.5 \leq Z \leq +3.5$, three of them are outliers so outside the range of the modified z-score and one is in a "border line zone" so questionable but still an acceptable value. One laboratory obtained an excellent value of modified z-score of 0.

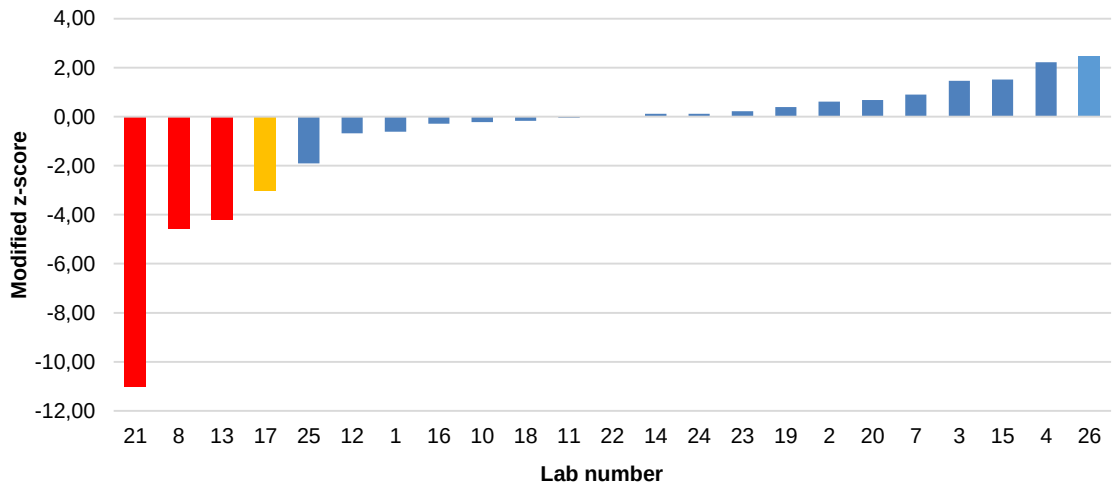


Figure 1. AMISULBROM: modified z-scores (ITPT2019)

For the identification of the outliers it was applied the Horwitz test in addition to the modified z-score, Figure 2 shows the percentage of Amisulbrom found for each laboratory, the median, the median +/- 2 MADe and the values of upper and lower Horwitz (*see* Glossary for details).

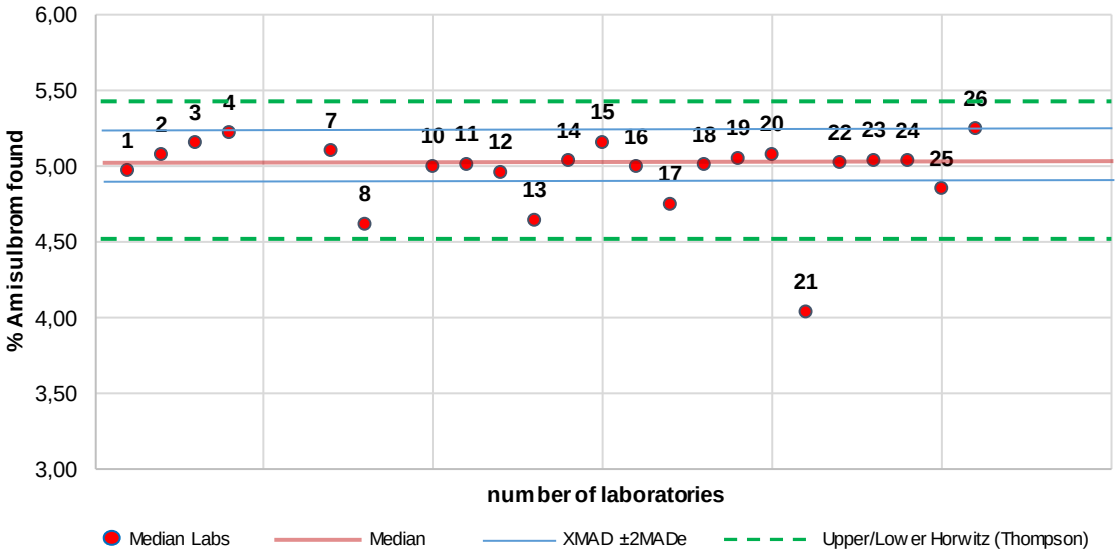


Figure 2. AMISULBROM: labs data summary (ITPT2019)

It is clear that 5 data are outside the lower median limit but 4 of them still inside the lower Horwitz limit and 1 outside it. Values up and down the median are equally distributed.

2.2. Dimethomorph

For the active substance Dimethomorph, 26 boxes were sent to all over Europe, in particular 10 to Italian's Laboratories and 16 to European Laboratories outside Italy. They have been received 25 participation results; the only one Laboratory missing is from Italy. All the laboratories, except for one who used the GC-FID, used for the analysis an LC instrument: 22 of them with a UV Detector and 2 with a MS Detector. To carry out this analysis 16 laboratories applied an in-house method, 9 the CIPAC method and no one used the manufacturer's method, as is showed in Table 9. At the same time, both the methods gave appreciable data, except for one laboratory who gave unacceptable values, as Figures 3 and 4 show.

Table 9. DIMETHOMORPH: methods applied for analysis (ITPT2019)

Laboratories	In-House	CIPAC	Manufacturer's
Number	16	9	0

As for the Amisulbrom, a statistical evaluation based on a robust estimator instead of the mean was applied on the collected data. The purpose of this choice was to cope the possibility of outlying data points without having to remove them, so it was used the median and the standard

deviation. Figure 3 shows the lab's values of modified z-score. The results obtained are valuable data, most of them are inside the z-score range of $-3.5 \leq Z \leq +3.5$ and one of them is completely unacceptable in in the positive zone and one is questionable. Only one of the laboratories obtained the excellent value of modified z-score of 0.

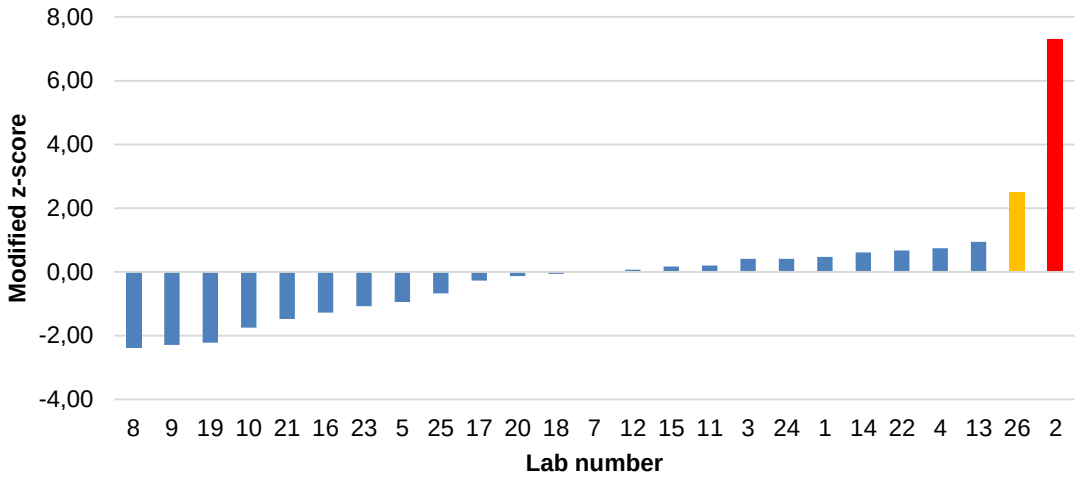


Figure 3. DIMETHOMORPH: modified z-scores (ITPT2019)

For the identification of the outliers it was applied the Horwitz test in addition to the modified z-score, Figure 4 shows the percentage of Dimethomorph found for each laboratory, the median, the median +/- 2 MADe and the values of upper and lower Horwitz (*see* Glossary for details).

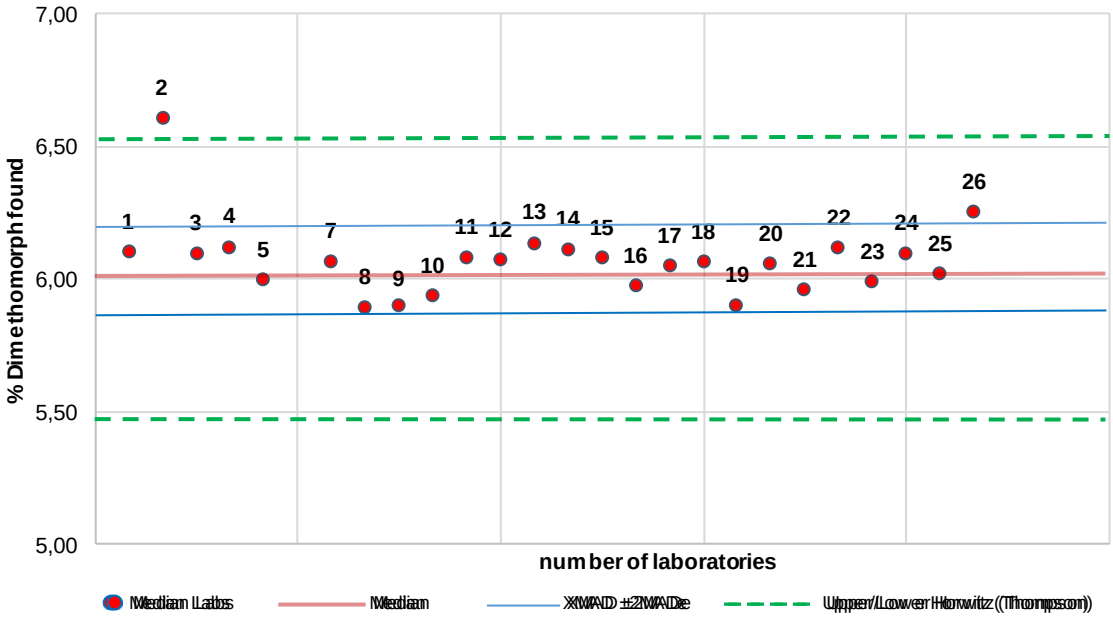


Figure 4. DIMETHOMORPH: labs data summary (ITPT2019)

Figure 4 shows that 1 data is outside the Upper Horwitz limit. There are 14 data up the median, 7 down the median bar and 2 have the same value of the median.

2.3. Pirimiphos-Methyl

Pirimiphos-Methyl was the third active substance and, as the other two, 26 boxes were sent to all over Europe, in particular 10 to Italian's Laboratories and 16 to European Laboratories outside Italy. They have been received 21 participation results; 3 Laboratories missing are from Italy and 2 are from outside Italy. The analysis was performed using LC instrument: 5 of them with a UV Detector and 2 with a MS Detector; 13 laboratories preferred to use GC-FID. Some of the laboratories choose to use an In-house method, others a CIPAC method and few others applied a manufacturer's method, as shown in Table 10. At the same time, all the methods gave appreciable data.

Table 10. PIRIMIPHOS-METHYL: methods applied for analysis (ITPT2019)

Laboratories	In-House	CIPAC	Manufacturer's
Number	15	5	1

A statistical evaluation based on a robust estimator (median) instead of the mean was applied on the collected data. The purpose of this choice was to cope the possibility of outlying data points without having to remove them, so it was used the median and the standard deviation.

As for the other two active substances mentioned before, a statistical evaluation based on a robust estimator instead the mean was applied on the collected data. The purpose of this choice was to cope the possibility of outlying data points without having to remove them, so it was used the median and the standard deviation. Figure 5 shows the lab's values of modified z-score. The results obtained are valuable data, most of them are inside the z-score range of $-3.5 \leq Z \leq +3.5$, two of them is completely unacceptable in the positive zone and one is questionable. Two of the laboratories obtained the excellent value of modified z-score of 0.

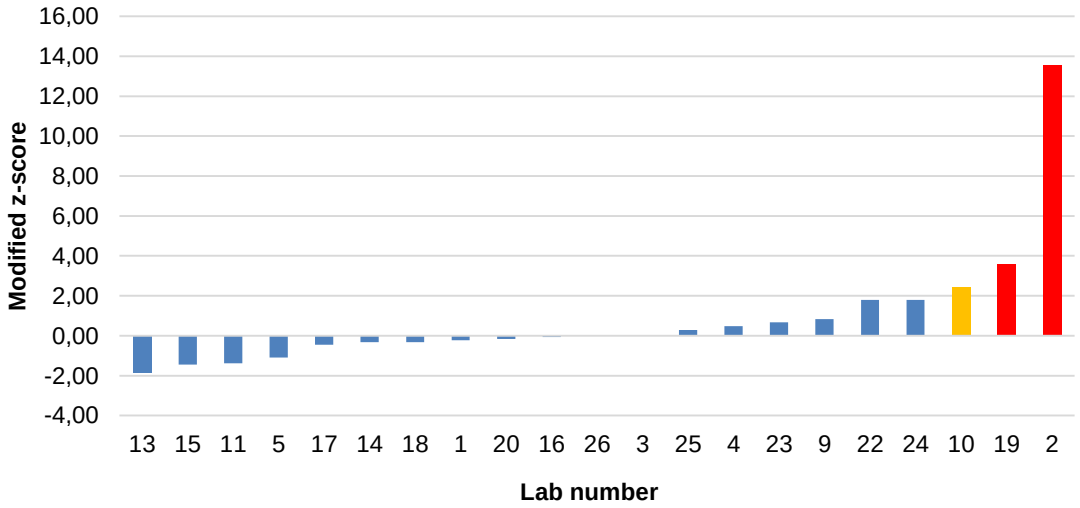


Figure 5. PIRIMIPHOS-METHYL: modified z-scores (ITPT2019)

For the identification of the outliers it was applied the Horwitz test in addition to the modified z-score, the plot n. 6 shows the percentage of Pirimiphos-Methyl found for each laboratories, the median, the median +/- 2 MADe and the values of upper and lower Horwitz (*see* Glossary for details).

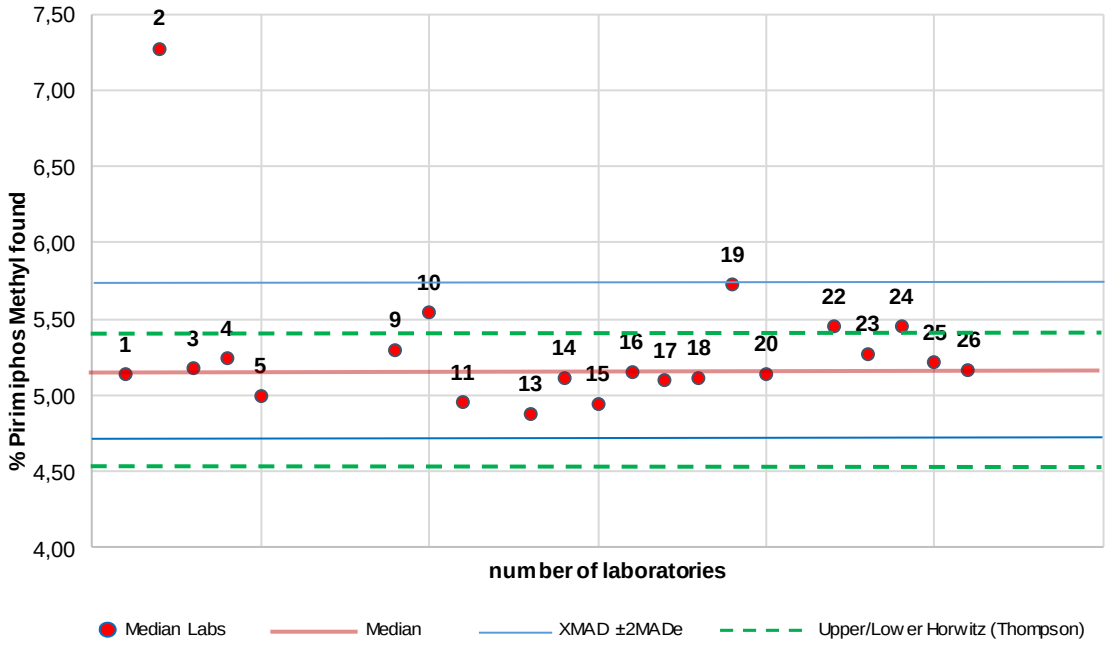


Figure 6. PIRIMIPHOS-METHYL: labs data summary (ITPT2019)

Figure 6 shows that there are 3 data outside the upper median limit, 5 data out the upper Horwitz bars. There are more values “under” the median than in the “upper” side: 5 data are up the median, 10 under to the median bar, and 1 has the same value of the median.

2.4. Propiconazole

Propiconazole was the fourth active substance and, as the other three mentioned before, 26 boxes were sent to all over Europe, in particular 10 to Italian’s Laboratories and 16 to European Laboratories outside Italy. They have been received 21 participation results; 4 Laboratories missing are from Italy and 1 is from outside Italy. The analysis was performed using LC instrument: 3 of them with a UV Detector and 4 with a MS Detector; 14 laboratories preferred to use GC-FID.

Some of the laboratories choose to use an In-house method, others a CIPAC method and few others applied a manufacturer’s method, as shown in Table 11. At the same time, all the methods gave appreciable data.

Table 11. PROPICONAZOLE: methods applied for analysis (ITPT2019)

Laboratories	In-House	CIPAC	Manufacturer's
Number	15	5	1

A statistical evaluation based on a robust estimator (median) instead the mean was applied on the collected data. The purpose of this choice was to cope the possibility of outlying data points without having to remove them, so it was used the median and the standard deviation.

As for the other two active substances, on the collected data it was applied a statistical evaluation based on a robust estimator instead the mean. The purpose of this choice was to cope the possibility of outlying data points without having to remove them, so it was used the median and the standard deviation.

Figure 7 shows the lab's values of modified z-score. The results obtained are valuable data, most of them are inside the z-score range of $-3.5 \leq Z \leq +3.5$, one of them is completely unacceptable in the positive zone and two of them are questionable. One laboratory obtained the excellent value of modified z-score of 0.

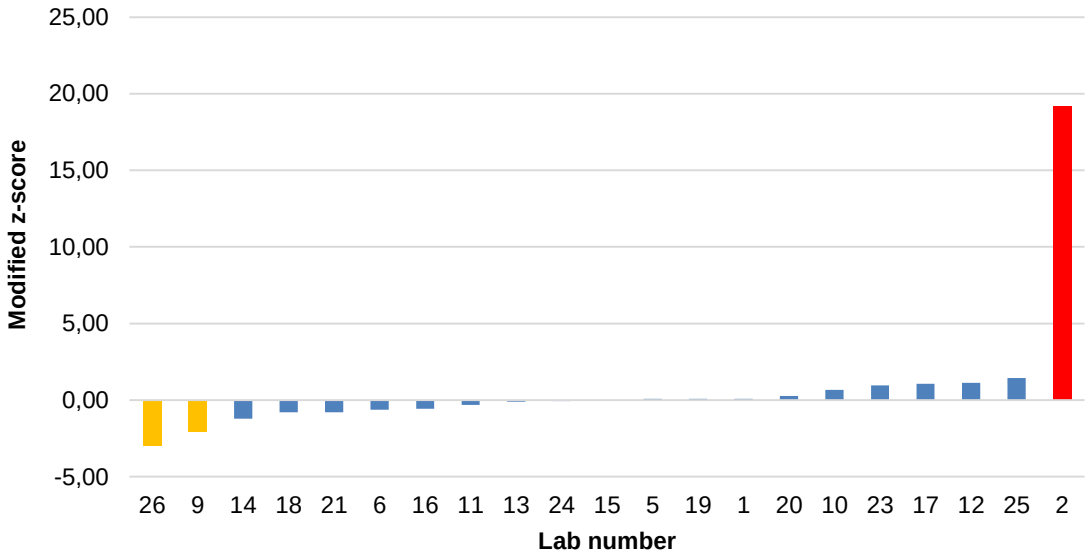


Figure 7. PROPICONAZOLE: modified z-scores (ITPT2019)

For the identification of the outliers it was applied the Horwitz test with the Thompson's correction in addition to the modified z-score, Figure 8 shows the percentage of Propiconazole found for each laboratory, the median, the median +/- 2 MADe and the values of upper and lower Horwitz. (*see* Glossary for details).

Figure 8 shows that there is 1 data outside the upper median and Upper Horwitz limit, 9 data out the upper median bar; 9 data are under the median bar. One has the same value of the median. One is out of the Lower Horwitz limit.

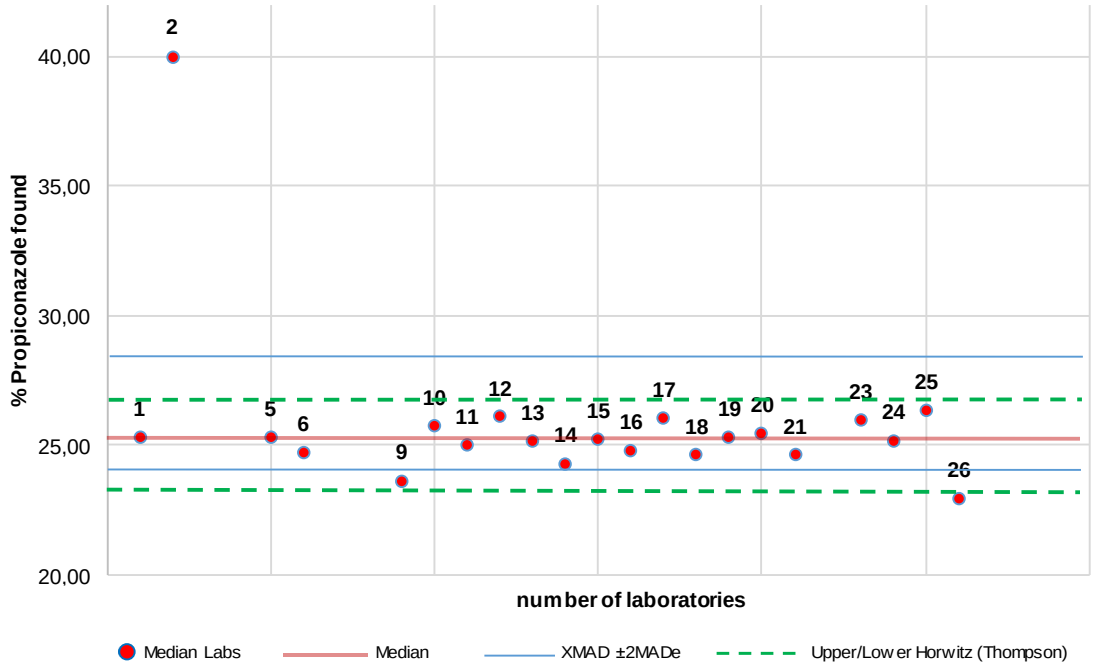


Figure 8. PROPICONAZOLE: labs data summary (ITPT2019)

3. RESULTS

The outcome of the ITPT2019 can be considered satisfactory due to the second PT organized by Italy.

The participation of the Italian and European laboratories was good. For Italy, ten laboratories participated distributed as four of the North, three in the Centre and two in the South of the Country. The European laboratories were sixteen, excluding Italy, distributed as one of the South, eleven of the Centre and four of the North of the Continent.

Tables 12, 13 and 14 summarize the participation per active ingredient and the results per active ingredient including and excluding the outliers.

For each active substance there were a percentage of failing results obtained with the modified z-score, as Table 12 shows.

Table 12. Summary of participation per active ingredient (ITPT2019)

ID Sample	Product description	Active ingredient	Participants (n.)	Labs using GC (n.)	Labs using LC (n.)	Failing results[1](%)
PPP01	Water dispersible granules	Amisulbrom	23	0	23	13.0
PPP02	Wettable powder	Dimethomorph	25	1	24	4.00
PPP03	Liquid	Pirimiphos-Methyl	21	14	7	9.52
PPP04	Emulsifiable concentrate	Propiconazole	21	16	5	4.76

[1] Where failing indicates a mean assay result outside the Horwitz defined acceptable limits.

Table 13. Summary of lab results per active ingredient, including outliers (ITPT2019)

ID Sample	Analyte (Label claim)	Minimum result	Maximum result	Grand Average	Grand %CV
PPP01	Amisulbrom 5%	4.04	5.32	4.96	5.23
PPP02	Dimethomorph 6%	5.66	6.76	6.07	2.68
PPP03	Pirimiphos-Methyl 5%	4.77	7.33	5.30	9.46
PPP04	Propiconazole 25%	22.6	43.2	25.8	13.2

Table 14. Summary of lab results per active ingredient, excluding outliers (ITPT2019)

ID Sample	Analyte (Label claim)	N. of outliers[1]	Average excluding outliers	%CV excluding outliers
PPP01	Amisulbrom 5%	3	5.04	2.24
PPP02	Dimethomorph 6%	1	6.05	1.45
PPP03	Pirimiphos-Methyl 5%	2	5.18	3.39
PPP04	Propiconazole 25%	1	25.1	3.29

[1] An outlier is flagged when the modified z-score falls outside the range of $-3.5 \leq Zi \leq 3.5$; see Appendix for calculations.

The performance of the laboratories expressed in terms of modified z-score was satisfactory by almost all participants for all substances. For each active substance there are outlier values, and the analysis of Amisulbrom was the most critical.

Almost all of the laboratories used the CIPAC methods for the four compounds or got inspired by the CIPAC method with some modification, for example, without using the internal standard.

One laboratory got 3 outliers of four analyses because it used a multiresidue instrumental method and this one probably has not good performance.

Based on the results it can be concluded that the PT was successfully organized also based on the number of participants. Details of the z-score values for each laboratory are given in Tables 15, 16, 17 and 18 with the analytical technique used for each substance.

Table 19, 20, 21 and 22 report the information on analytical methods used for each substance and each laboratory.

Table 15. AMISULBROM sample PPP01: summary results (ITPT2019)

ID Lab	Analytical technique	Two day average[1]	RPD[1]	Modified z- score[2]	Outlier[2]
1	LC-DAD	4.97	0.00	-0.62	no
2	LC-QQQ	5.08	-0.05	0.62	no
3	LC-UV/Vis PDA	5.15	-0.03	1.46	no
4	LC-DAD	5.22	0.03	2.23	no
7	LC-DAD	5.10	0.02	0.90	no
8	LC-DAD	4.62	-0.02	-4.55	yes
10	LC-UV	5.00	0.02	-0.22	no
11	LC-PDA	5.02	0.01	-0.06	no
12	LC-DAD	4.96	-0.01	-0.67	no
13	LC-DAD	4.65	0.02	-4.22	yes
14	LC-DAD	5.03	-0.01	0.11	no
15	LC-DAD	5.16	0.01	1.52	no
16	LC-Dionex UVD	5.00	0.00	-0.28	no
17	LC-PDA	4.75	0.02	-3.04	no
18	LC-DAD	5.01	0.01	-0.17	no
19	LC-DAD	5.06	0.01	0.39	no
20	LC-DAD	5.08	0.00	0.67	no
21	LC-UV	4.04	0.00	-11.02	yes
22	LC-PDA	5.02	0.00	0.00	no
23	LC-UVD	5.04	-0.01	0.22	no
24	LC-DAD	5.03	-0.01	0.11	no
25	LC-UV	4.85	-0.04	-1.91	no
26	LC-DAD	5.24	0.03	2.47	no

Lower Horwitz[3]	4.56
Upper Horwitz[3]	5.44
Grand Average[4]	4.96
Total SD	0.25
Total Median[5]	5.02
MAD	0.06
MAD_E	0.09

[1] Average yield and Relative Percent Difference between the two-day determinations per laboratory.

[2] An outlier is flagged when the modified z-score falls outside the range of $-3.5 \leq Zi \leq 3.5$; see Glossary.

[3] Based on ITPT-01 results, Horwitz limits for uniform samples based on median yield.

[4] Grand average, standard deviation and median.

[5] Median Absolute Deviation Robust estimate of standard deviation; see Glossary for calculations.

Table 16. DIMETHOMORPH sample PPP02: summary results (ITPT2019)

ID Lab	Analytical technique	Two day average[1]	RPD[1]	Modified z-score[2]	Outlier[2]
1	LC-DAD	6.11	4.10	0.47	no
2	LC-QQQ	6.61	-4.54	7.28	yes
3	LC-UV/Vis PDA	6.10	-0.33	0.40	no
4	LC-DAD	6.13	1.47	0.74	no
5	GC-QQQ	6.00	0.00	-0.94	no
7	LC-DAD	6.07	0.66	0.00	no
8	LC-DAD	5.90	0.17	-2.36	no
9	LC-DAD	5.90	6.78	-2.29	no
10	LC-UV	5.94	-0.34	-1.75	no
11	LC-PDA	6.09	0.49	0.20	no
12	LC-DAD	6.08	0.82	0.07	no
13	LC-DAD	6.14	2.93	0.94	no
14	LC-DAD	6.12	1.80	0.61	no
15	LC-DAD	6.08	-0.21	0.17	no
16	LC- Dionex UVD	5.98	0.50	-1.28	no
17	LC-PDA	6.05	1.65	-0.27	no
18	LC-DAD	6.07	0.82	-0.07	no
19	LC-DAD	5.91	-0.17	-2.23	no
20	LC-DAD	6.06	0.99	-0.13	no
21	LC-UV	5.96	10.07	-1.48	no
22	LC-DAD	6.12	4.90	0.67	no
23	GC-FID	5.99	1.00	-1.08	no
24	LC-DAD	6.10	0.98	0.40	no
25	LC- UV	6.02	0.00	-0.67	no
26	LC-DAD	6.26	-3.68	2.50	no

Lower Horwitz[3]	5.48
Upper Horwitz[3]	6.52
Grand Average[4]	6.07
Total SD	0.14
Total Median[5]	6.07
MAD	0.05
MAD_E	0.07

[1] Average yield and Relative Percent Difference between the two-day determinations per laboratory.
[2] An outlier is flagged when the modified z-score falls outside the range of $-3.5 \leq Zi \leq 3.5$; see Glossary.
[3] Based on ITPT-01 results, Horwitz limits for uniform samples based on median yield.
[4] Grand average, standard deviation and median.
[5] Median Absolute Deviation Robust estimate of standard deviation; see Glossary for calculations.

Table 17. PIRIMIPHOS-METHYL sample PPP03: summary results (ITPT2019)

ID Lab	Analytical technique	Two day average[1]	RPD[1]	Modified z-score[2]	Outlier[2]
1	GC-FID	5.135	0.19	-0.22	no
2	LC-QQQ	7.28	1.37	13.55	yes
3	LC-UV/Vis PDA	5.175	-5.22	0.03	no
4	LC-DAD	5.245	4.39	0.48	no
5	LC-MS/MS QQQ	5	0.00	-1.09	no
9	GC-MS	5.3	-3.77	0.84	no
10	LC-UV	5.545	0.18	2.41	no
11	GC-FID	4.955	-0.61	-1.38	no
13	LC-DAD	4.88	4.51	-186	no
14	GC-FID	5.12	-3.13	-0.32	no
15	GC-FID	4.945	-1.42	-1.45	no
16	GC-FID	5.16	-0.78	-0.06	no
17	GC-FID	5.1	0.00	-0.45	no
18	GC-FID	5.12	0.39	-0.32	no
19	GC-FID	5.725	1.57	3.57	yes
20	GC-FID	5.145	0.19	-0.16	no
22	LC-PDA	5.45	-3.67	1.80	no
23	GC-FID	5.275	2.09	0.67	no
24	GC-FID	5.45	0.37	1.80	no
25	GC-FID	5.215	-1.34	0.29	no
26	GC-FID	5.17	5.80	0.00	no

Lower Horwitz[3]	4.56
Upper Horwitz[3]	5.44
Grand Average[4]	5.30
Total SD	0.50
Total Median[5]	5.17
MAD	0.11
MAD_E	0.16

[1] Average yield and Relative Percent Difference between the two-day determinations per laboratory.
[2] An outlier is flagged when the modified z-score falls outside the range of $-3.5 \leq Zi \leq 3.5$; see Glossary.
[3] Based on ITPT-01 results, Horwitz limits for uniform samples based on median yield.
[4] Grand average, standard deviation and median.
[5] Median Absolute Deviation Robust estimate of standard deviation; see Glossary for calculations.

Table 18. PROPICONAZOLE sample PPP04: summary results (ITPT2019)

ID Lab	Analytical technique	Two day average[1]	RPD[1]	Modified z-score[2]	Outlier[2]
1	GC-FID	25.3	0.00	0.09	no
2	LC-QQQ	40	-16.00	19.92	yes
5	GC-QQQ	25.3	-3.16	0.09	no
6	GC-MS	24.75	14.95	-0.65	no
9	GC-FID	23.65	1.27	-2.14	no
10	LC-UV	25.75	-0.39	0.70	no
11	GC-FID	25	1.60	-0.31	no
12	LC-DAD	26.1	-2.30	1.17	no
13	GC-MS	25.15	12.33	-011	no
14	GC-FID	24.3	1.65	-1.26	no
15	GC-FID	25.233	0.29	0.00	no
16	GC-FID	24.8	0.81	-0.58	no
17	GC-FID	26.05	-2.69	1.10	no
18	GC-FID	24.615	-4.18	-0.83	no
19	GC-FID	25.3	0.79	0.09	no
20	GC-FID	25.45	-0.39	0.29	no
21	LC-UV	24.625	1.10	-0.82	no
23	GC-FID	25.98	-4.77	1.01	no
24	GC-FID	25.18	-0.16	-0.07	no
25	GC-FID	26.35	0.38	1.51	no
26	GC-FID	22.95	-3.05	-3.08	no

Lower Horwitz[3]	23.26
Upper Horwitz[3]	26.74
Grand Average[4]	25.80
Total SD	3.41
Total Median[5]	25.23
MAD	0.52
MAD_E	0.77

[1] Average yield and Relative Percent Difference between the two-day determinations per laboratory.

[2] An outlier is flagged when the modified z-score falls outside the range of $-3.5 \leq Zi \leq 3.5$; see Glossary.

[3] Based on ITPT-01 results, Horwitz limits for uniform samples based on median yield.

[4] Grand average, standard deviation and median.

[5] Median Absolute Deviation Robust estimate of standard deviation; see Glossary for calculations.

Table 19. AMISULBROM: representative method for the determination (ITPT2019)

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume	Column T°	Detector	Column
1	In-house method	Acetofenone	Acetonitrile	Sonicate for 15 min. Filter through 0.45 µm, nylon	20 µL	40°C	DAD	Zorbax ODS Agilent 5 µm, 150 mm x 4.6 mm
2	In-house method	Malathion D6	Methanol	N/A	5 µL	25°C	Triple Quadru pole	Hypersil Gold 1.9 µm, 50 mm x 2.1 mm
3	In-house method	N/A	Methanol: Water (90:10 v/v)	Sonicate for 15 min Filter 0.45 µm	20 µL	25°C	UV/Vis PDA	Thermo Fischer Acquasil C18 5 µm, 150 mm x 2.1 mm
4	CIPAC 789	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Sonicate for 10 min Filter through 0.45 µm PTFE disk	5 µL	40°C	DAD	Restek Pinnacle II C18 5 µm, 150 mm x 4.6 mm
7	In-house method	N/A	Acetonitrile	Sonicate for 15 min Filter through 0.45 µm nylon disk	10 µL	35°C	DAD	Agilent Zorbax Eclipse XDB C8 5 µm, 15 mm x 4.6 mm
8	CIPAC 789	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Manual agitation, sonication and filtration	5 µL	30°C	DAD	BDS Hypersil C18 5 µm, 150 mm x 4.6 mm
10	In-house method	N/A	Acetonitrile	Sonicate for 5 min	2 µL	30°C	UV	XTerra RP18 3.5 µm, 150 mm x 2.1 mm
11	Manufacturer's method	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Sonicate for 10 min Filter through a 0.45 µm, PTFE filter	5 µL	40°C	PDA	Phenomenex Prodigy OSD-3 5 µm, 250 mm x 4.6 mm
12	CIPAC 789	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Ultrasonication for 10 min	5 µL	40°C	DAD	Kintex C18 5 µm, 150 mm x 4.6 mm
13	In-house method	N/A	Water: Tetrahydrofuran (50:50 v/v)	Sonicate for 30 min Filter through 0.2 µm, PP disk	10 µL	35°C	DAD	Nucleodur C18 5 µm, 250 mm x 3 mm
14	In-house method	N/A	Acetonitrile	Sonicate for 15 min Filter through 0.45 µm regenerated cellulose disk	5 µL	40°C	DAD	LiChrospher 100 RP18 5 µm, 250 mm x 4mm

to be followed

continues

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume	Column T°	Detector	Column
15	CIPAC 789	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Sonicate for 1 min Filter through 0.2 µm PTFE filter	5 µL	40°C	DAD	Nucleodur Gravity C18 5 µm, 250 mm x 4,6 mm
16	In-house method	N/A	Acetonitrile	Sonicate for 15 min Shake for 20 min at 120 strokes/min	5 µL	25°C	Dionex UVD 170S	Zorbax SB-C18 5 µm, 250 mm x 4.6 mm
17	In-house method	N/A	Water:Acetonitrile (10:90 v/v)	Sonicate for 5 min Filter 0.45 µm, nylon disk	5 µL	25°C	PDA	Phenomenex Kinetix C18 2.6 µm, 100 mm x 4.6 mm
18	In-house method	N/A	Acetonitrile	Sonicate for 1 min Filter through 0.45 µm PTFE filter	5 µL	40°C	DAD	Altima C18 5 µm, 250 mm x 4.6 mm
19	In-house method	N/A	Water: Methanol (5:95 v/v)	Sonicate for 1 min Filter 0.2 µm nylon disk	2 µL	40°C	DAD	Phenomenex Kinetex C18 2.6 µm, 100 mm x 4.6 mm
20	CIPAC 789	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Sonicate for 15 min Filter through 0.45 µm PTFE filter	5 µL	40°C	DAD	Zorbax Eclipse XDB-C18 5 µm, 250 mm x 4.6 mm
21	CIPAC 789	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Sonicate for 1 min	5 µL	40°C	UV	Spherisorb S5 ODS 2 C18 5 µm, 250 mm x 4.6 mm
22	Manufacturer's method	Propio-phenone	Acetonitrile	Sonicate for 20 min Filter through 0.2 µm nylon disk	1 µL	40°C	PDA	BEH C18 Waters 1.7 µm, 50 mm x 2.1 mm
23	CIPAC 789	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Sonicate for 10 min	5 µL	40°C	UVD	Lichrospher 100-5 RP-18 5 µm, 250 mm x 4 mm
24	CIPAC 789	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Filter through 0.2 µm PTFE filter	10 µL	40°C	DAD	Zorbax SB C18 5 µm, 250 mm x 4.6 mm
25	In-house method	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Sonicate for 20 min Filter through 0.45 µm and 0.2 µm PTFE	5 µL	40°C	UV	Agilent Zorbax Eclipse Plus C18 5 µm, 250 mm x 4.6 mm
26	CIPAC 789	N/A	Acetonitrile: H_20 0.01% H_3PO_4 (75:25 v/v)	Sonicate for 1 min Filter through 0.2 µm PTFE filter	5 µL	40°C	PDA	Hypersil Gold 5 µm, 250 mm x 4mm

Table 20. DIMETHOMORPH: representative method for the determination (ITPT2019)

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume	Column T°	Detector	Column
1	In-house method	Acetofenone	Acetonitrile	Sonicate for 15 min Filter through 0.45 µm nylon disk	20 µL	40°C	DAD	ZORBAX SB-C18 5 µm, 250 mm x 4.6 mm
2	In-house method	Malathion D6	Methanol	N/A	5 µL	25°C	Triple Quadrupole	Hypersil Gold 1.9 µm, 50 mm x 2.1 mm
3	In-house method	N/A	Methanol: Water (90:10 v/v)	Sonicate for 15 min Filter 0.45 µm	20 µL	25°C	UV/Vis PDA	Thermo Fischer Acquasil C18 5 µm, 150 mm x 2.1 mm
4	CIPAC 483	N/A	Acetonitrile	Sonicate for 10 min Filter through 0.45 PTFE disk	10 µL	22°C	DAD	Restek Pinnacle II C18 5 µm, 150 mm x 4.6 mm
5	In-house method	Triphenyl-phosphate	Acetonitrile	Sonicate for 10 min	10 µL	40°C	MS/MS QQQ	Ascentis Express RP-AMIDE 2.7 µm, 150 mm x 2.1 mm
7	In-house method	N/A	Acetonitrile	Sonicate for 15 min Filter through 0.45 µm nylon disk	10 µL	35°C	DAD	Agilent Zorbax Eclipse XDB C8 5 µm, 15 mm x 4.6 mm
8	CIPAC 483	N/A	Acetonitrile: Water (45:55 v/v)	Agitate manually, Centrifugate	5 µL	30°C	DAD	BDS Hypersil C18 5 µm, 150 mm x 4.6 mm
9	CIPAC 483	N/A	Acetonitrile	Sonicate for 3 min, Centrifugate, Filter on 0.45 µm nylon membrane	25 µL	25°C	DAD	Zorbax Eclipse XDB C18 3.5 µm, 150 mm x 2.1 mm
10	In-house method	N/A	Acetonitrile	Sonicate for 5 min	2 µL	30°C	UV	XTerra RP18 3.5 µm, 150 mm x 2.1 mm
11	In-house method	N/A	Acetonitrile: Water (40:60 v/v)	Sonicate for 10 min Filter through a 0.45 µm PTFE filter	10 µL	25°C	PDA	Hypersil ODS 5 µm, 250 mm x 4 mm
12	CIPAC 483	N/A	Water: Acetonitrile	Ultrasonicate for 3 min + ultrasonicate 5 min	10 µL	22°C	DAD	Kintex C18 5 µm, 150 mm x 4.6 mm
13	In-house method	N/A	Water: Tetrahydrofuran (50:50 v/v)	Sonicate for 30 min Filter through 0.2 µm PP disk	10µL	35°C	DAD	Nucleodur C18 5 µm, 250 mm x 3 mm

to be followed

continues

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume	Column T°	Detector	Column
14	In-house method	N/A	Acetonitrile	Sonicate for 15 min Filter through 0.45 µm Regenerated cellulose disk	2 µL	55°C	DAD	Zorbax Eclipse XDB C18 1.8 µm, 50 mm x 4.6 mm
15	CIPAC 483	N/A	Acetonitrile	Sonicate for 3 min	10 µL	40°C	DAD	Nucleodur Gravity C18 5 µm, 250 mm x 4.6 mm
16	In-house method	N/A	Acetonitrile	Sonicate for 15 min, Shake for 20 min at 120 strokes/min	5 µL	25°C	Dionex UVD 170S	Zorbax SB-C18 5 µm, 250 mm x 4.6 mm
17	In-house method	N/A	Water: Acetonitrile (10:90 v/v)	Sonicate for 5 min Filter 0.45 µm nylon disk	5 µL	25°C	PDA	Phenomenex Kinetix C18 2.6 µm, 100 mm x 4.6 mm
18	In-house method	N/A	Acetonitrile	Sonicate for 3 min Filter through 0.45 µm PTFE filter	5 µL	22°C	DAD	YMC J'SPHERE ODS-H80 4 µm, 250 mm x 4.6 mm
19	In-house method	N/A	Water: Methanol (5:95 v/v)	Sonicate for 1 min Filter 0.2 µm nylon disk	2 µL	40°C	DAD	Phenomenex Kinetex C18 2.6 µm, 100 mm x 4.6 mm
20	CIPAC 483	N/A	Acetonitrile	Sonicate for 15 min Filter through 0.45 µm PTFE filter	10 µL	20°C	DAD	Zorbax Eclipse XDB-C18 5 µm, 4.6 mm x 150 mm
21	In-house method	N/A	Water: Acetonitrile (5:95 v/v)	Sonicate for 3+5 min	20 µL	40°C	UV	Spherisorb S5 ODS 2 C18 5 µm, 250 mm x 4.6 mm
22	CIPAC 483	N/A	Acetonitrile	Sonicate for 30 min Filter through 0.2 µm nylon disk	1 µL	30°C	PDA	HSS T3 Waters 1.8 µm, 100 mm x 2.1 mm
23	In-house method	Hexyl Benzoate	Acetonitrile	Sonicate for 20 min	1 µL	275°C	FID	HP-5 5% phenylmethylsiloxane 0.25µm, 30 m x 0.32 mm
24	In-house method	Methyl-4-hydroxybenzoate	Acetonitrile	Sonicate for 8 min Filter through 0.22 µm PTFE filter	10 µL	25°C	DAD	Hypersil ODS 3 µm, 125 mm x 4.0 mm
25	In-house method	N/A	Acetonitrile	Sonicate for 20 min Filter through 0.45 µm PTFE filter	10 µL	25°C	UV	Agilent Zorbax Eclipse Plus C18 5 µm, 250 mm x 4.6 mm
26	CIPAC 483	N/A	Acetonitrile	Sonicate for 3 min Filter through 0.45 µm PTFE filter	10 µL	22°C	DAD	Intersil ODS-4 5 µm, 250 mm x 4.6 mm

Table 21. PIRIMIPHOS METHYL: representative method for the determination (ITPT2019)

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume	Column T°	Detector	Column
1	In-house method	Bis-butilftalato	Acetone	Sonicate for 15 min	1 µL	250°C	FID	5% Phenyl Methyl Siloxane 25 µm, 30 m x 0.25 mm
2	In-house method	N/A	Acetonitrile	N/A	5 µL	25°C	QQQ	Hypersil Gold 1.9 µm, 50 mm x 2.1 mm
3	In-house method	N/A	Methanol: Water (90:10 v/v)	Filter through 0.45 µm	20 µL	25°C	UV/Vis PDA	Thermo Fischer Acquasil C18 5 µm, 150 mm x 2.1 mm
4	In-house method	N/A	Acetone	Filter through 0.45 µm PTFE disk	10 µL	30°C	DAD	Restek Pinnacle II C18 5 µm, 150 mm x 4.6 mm
5	In-house method	Triphenyl-phosphate	Acetonitrile	Sonicate for 10 min	10 µL	40°C	QQQ	Ascentis Express RP-AMIDE 2.7 µm, 150 mm x 2.1 mm
9	CIPAC 239	N/A	Acetone	N/A	1 µL	170°C	MS	SPB-5 0.25 µm, 30 m x 0.25 mm
10	In-house method	N/A	Acetonitrile	Sonicate for 5 min	2 µL	30°C	UV	XTerra RP18 3.5 µm, 150 mm x 2.1 mm
11	CIPAC 239	4,4-Dimethoxy-benzo-phenone	Acetone	Sonicate for 5 min Filter through 0.45 µm PTFE filter	1 µL	170°C	FID	HP-1 0.25 µm, 30 m x 0.25 mm
13	In-house method	N/A	Water: Tetrahydrofuran (50:50 v/v)	Sonicate for 30 min Filter through 0.2 µm PP disk	10 µL	35°C	DAD	Nucleodur C18 5 µm, 250 mm x 3 mm
14	In-house method	N/A	Acetone	Sonicate for 15 min	1 µL	250°C	FID	Zebron 7HM-G-006 ZB-17-01 0.25 µm, 30 m x 0.32 mm
15	In-house method	Dicyclohexyl phthalate	Acetone	Sonicate for 5 min	1 µL	170°C	FID	DB-1 1.5 µm, 30 m x 0.53 mm
16	In-house method	Diphenylphthalate	Acetone	Sonicate for 15 min Shake for 20 min at 120 strokes/min	1 µL	250°C	FID	VF-1ms 0.25 µm 15 m x 0.25 mm

to be followed

continues

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume	Column T°	Detector	Column
17	In-house method	N/A	Ethyl Acetate	N/A	0.2 µL	250°C	FID	DB 5 MS 0.25 µm, 30 m x 0.25 mm
18	In-house method	N/A	Acetone	Sonicate for 3 min Filter through 0.45 µm PTFE filter	1 µL	300°C	FID	HP-5MS UI 0.25 µm, 30 m x 250 mm
19	In-house method	Dipropyl-phthalate	Acetone	N/A	1 µL	270°C	FID	DB-1 0.25 µm, 30 m x 0.25 mm
20	CIPAC 239	4,4-Dimethoxy-benzo-phenone	Acetone	Sonicate for 15 min	1 µL	270°C	FID	DB-1 0.25 µm, 30 m x 0.25 mm
22	In-house method	N/A	Acetonitrile	Sonicate for 15 min Filter through 0.2 µm nylon disk	1 µL	40°C	PDA	BEH C18 Waters 1.7 µm, 50 mm x 2.1 mm
23	Manufacturer's method	Eicosane	Acetone	Sonicate for 20 min	1 µL	300°C	FID	HP-5 5% phenylmethylsiloxane 0.25 µm, 30 m x 0.32 mm
24	In-house method	N/A	Acetone	Sonicate for 2 min	1 µL	170°C	FID	DB-1 0.25 µm, 15 m x 0.25 mm
25	In-house method	Benzo-phenone	Acetone	Sonicate for 20 min Filter through 0.45 µm PTFE filter	1 µL	170°C	FID	ATTM-5 0.32 µm, 30 m x 25 mm
26	CIPAC 239	4,4 Dimethoxy-benzo-phenone	Acetone	Sonicate for 5 min Filter through 0.45 µm PTFE filter	1 µL	170°C	FID	DB-1 0.25 µm 30 m x 0.25 mm

Table 22. PROPICONAZOLE: representative method for the determination (ITPT2019)

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume	Column T°	Detector	Column
1	In-house method	Di-(2-ethylhexyl)phthalate	Acetone	Sonicate for 15 min	1 µL	250°C	FID	5% Phenyl Methyl Siloxane 0.25 µm, 30 m x 0.25 mm
2	In-house method	N/A	Acetonitrile	N/A	5 µL	25°C	QQQ	Hypersil Gold 1.9 µm, 50 mm x 2.1 mm
5	In-house method	Triphenyl-phosphate	Acetonitrile	Sonicate for 10 min	10 µL	40°C	MS/MS QQQ	Ascentis Express RP-AMIDE 2.7 µm, 150 mm x 2.1 mm
6	In-house method	N/A	Acetone	Sonicate for 10 min	2 µL	55°C	MS	DB17 0.25 µm, 30 m x 0.25 mm
9	CIPAC 408	N/A	Methyl Ethyl Ketone	N/A	1 µL	220°C	FID	ZB-WAX 0.25 µm, 30 m x 0.25 mm
10	In-house method	N/A	Acetonitrile	Sonicate for 5 min	2 µL	30°C	UV	XTerra RP18 3.5 µm, 150 mm x 2.1 mm
11	In-house method	Docosane	Acetone	Sonicate for 5 min Filter through 0.45 µm PTFE filter	1 µL	280°C	FID	HP-5 0.25 µm, 30 m x 0.25 mm
12	In-house method	N/A	Water/Acetonitrile	Ultrasonicate for 15 min	10 µL	30°C	DAD	Kintex C18 5 µm, 150 mm x 4.6 mm
13	In-house method	4,4'-Dibromo-biphényl	Acetone/ Tetrahydrofuran (50:50 v/v)	Sonicate for 15 min Filter through 0.45 µm PP disk	1 µL	250°C	MS	ZB-5MS 0.1 µm, 10 m x 0.1 mm
14	In-house method	N/A	Acetone	Sonicate for 15 min	1 µL	250°C	FID	Zebron 7HM-G-006 ZB-17-01 0.25 µm, 30 m x 0.32 mm
15	CIPAC 408	Di-(2-ethylhexyl)-phthalate	Methyl Isobutyl Ketone	N/A	1 µL	250°C	FID	DB-1 1.5 µm, 30 m x 0.53 mm
16	In-house method	Diphenyl-phthalate	Acetone	Sonicate for 15 min Shake for 20 min at 120 strokes/min	1 µL	250°C	FID	VF-1ms 0.25 µm 15 m x 0.25 mm

to be followed

continues

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume	Column T°	Detector	Column
17	In-house method	N/A	Ethyl Acetate	N/A	0.2 µL	250°C	FID	DB 5 MS 0.25 µm, 30 m x 0.25 mm
18	In-house method	N/A	Acetone	Sonicate for 3 min Filter through 0.45 µm PTFE filter	1 µL	300°C	FID	HP-5MS UI 0.25 µm, 30 m x 250 mm
19	In-house method	Diisobutyl-phthalate	Acetone	N/A	1 µL	280°C	FID	DB-1 0.25 µm, 30 m x 0.25 mm
20	In-house method	N/A	Acetone	Sonicate for 15 min	1 µL	220°C	FID	DB-5 0.25 µm, 30 m x 0.25 mm
21	In-house method	N/A	Ethanol	N/A	20 µL	N/A	UV	Spherisorb S5 ODS 2 C18 5 µm, 250 mm x 4.6 mm
23	Manufacturer's method	DIOP	Acetone	N/A	1 µL	285°C	FID	HP-5 5% phenylmethylsiloxane 0.25 µm, 30 m x 0.32 mm
24	CIPAC 408	Docosane	Acetone	Sonicate for 2 min Filter through 0.22 µm PTFE syringe filter	1 µL	250°C	FID	TG-5MS 1 µm, 15 m x 0.32 mm
25	CIPAC 408	Di-(2-ethylhexyl) phthalate	Methyl Isobutyl Ketone	Sonicate for 20 min Filter through 0.45 µm PTFE filter	1 µL	240°C	FID	ATTM-5 0.32 µm, 30 m x 25 mm
26	CIPAC 408	Di-(2-ethylhexyl) phthalate	Methyl Isobutyl Ketone	Sonicate for 2 min Filter through 0.45 µm PTFE filter	1 µL	240°C	FID	DB-5 0.25 µm 30 m x 0.25 mm

REFERENCES

Association of American Pesticide Control Officials. *Pesticide formulations checks sample program.* West Lafayette; AAPCO; 2016.

ISO/IEC 13528:2015. *Statistical methods for use in proficiency testing by interlaboratory comparison*. Geneva: International Organization for Standardization; 2015

ISO/IEC 17025:2018. *General requirements for the competence of testing and calibration laboratories*. Geneva: International Organization for Standardization; 2018.

Rivera CP, Rodríguez RD, Pimentel SH. Horwitz equation as quality benchmark in ISO/IEC 17025 Testing Laboratory. In: *Conference proceedings*; 2011.

Thompson M, Ellison SLR, Wood R. The International Harmonized Protocol for the Proficiency testing of analytical chemistry laboratories (IUPAC Technical Report). *Pure Appl Chem* 2006;78(1):145-96.

APPENDIX A
The announcement letter

ANNOUNCEMENT/INVITATION
ITPT2019

Dear Colleagues,

We herewith cordially invite you to participate in the Italian Proficiency Test on the analysis of PPPs in WG, WP, L, EC. This exercise is organized by the Italian Laboratory of Istituto Superiore di Sanità (National Institute of Health) – Department of Environment and Health. The ITPT2019 is scheduled to run from 15th January until 30th April 2019.

AIMS
Participation in proficiency tests is part of the QA/QC system of laboratories and provides them with an assessment of their analytical performance as well as a comparison with the performance of other laboratories. The general aim is to help laboratories demonstrate adequate analytical performance and, in case of underperformance, to help them identify sources of errors so that the necessary measures for quality improvement can be taken.

TEST ITEM
Ca. 10 g of PPP Test Item will be delivered to each participating lab.

TARGET ANALYTES
The analytes are: Amisulbrom WG, Dimethomorph WP, Pirimiphos-Methyl L, Propiconazole EC.

SHIPMENT AND RECEIPT OF THE TEST ITEM
The shipment of the Test Item is planned to start on 15th January 2019. If any laboratory will be on holiday in the week of the shipment, please inform the organizer to rearrange shipment.
Participants must check the integrity and condition of the materials upon receipt and to report within 48 h if they accept the materials or not.

IMPORTANT DATES
- The shipment of the Test Items is planned to start on 15th January 2019.
- Submission of results and method information should be done by 30th April 2019.

PARTICIPATION FEE
The participation is free of charge.

RELEVANT DOCUMENTS
Participants are encouraged to employ the method typically run in their lab for these analytes.

SUPPORT AND CONTACT INFORMATION
For any questions about the ITPT2019, please mail to
angela.santilio@iss.it or chiara.pompili@iss.it

Best regards,

The ITPT2019 Organizing Team

APPENDIX B
Calendar and list of participants

CALENDAR for the ITPT2019

Activity	Dates
Opening of the ITPT2019	6th November 2018
Confirm the participation	30th November 2018
Shipment of the ITPT2019 Test Item	15th January 2019
Confirmation of Sample Receipt and Acceptance	Within 48 h of receipt
Result Submission	30th January – 30th April 2019
Preliminary Report	May 2019
Final Report	June 2019

LIST OF PARTICIPANTS

Italian participants

Cecilia Capannesi	*Laboratorio Sanità Pubblica, Firenze*
Luca D'Ambrosio	*Agenzia Provinciale per l'Ambiente – Bolzano*
Francesca Ferrieri	*Polo Alimenti ARPA Puglia*
Marco Morelli	*ARPA Emilia Romagna* *Sede secondaria laboratorio Multisito, sezione di Ferrara*
Leonardo Sabatino	*Ministero delle Politiche Agricole Alimentari e Forestali, Ispettorato centrale della tutela della qualità e repressione frodi dei prodotti agroalimentari - Laboratorio di Catania*
Antonella Salzarulo	*ARPA Piemonte – Laboratorio Specialistico Nord Ovest*
Chiara Pompili	*Istituto Superiore di Sanità, Roma*
Pierangela Rovellini	*INNOVHUB – SSOG, Milano*
Andrea Vantini	*ARPA Veneto, Verona*

European participants

Lajos Sándor Benke	*National Food Chain Safety Office – Hungary*
Florentina Ciotea	*National Phytosanitary Authority - Romania*
Amelie Coste	*Service Commun des Laboratories – Lyon, France*
Frantisek Csicsay	*ÚKSÚP – Bratislava, Slovakia*
Christoph Czerwenka	*AGES GmbH – Wien, Austria*
Kristina Dürkop	*Federal Office of Consumer Protection and Food Safety – Braunschweig, Germany*
Jim Garvey	*The Pesticide Laboratory Control – Backweston, Ireland*
Kati Hakala	*Finnish Food Safety Authority EVIRA – Helsinki, Finland*
Eva Jacobsen	*Danish Technological Institute – Aarhus, Denmark*
Helen Karasali	*Benaki Phytopathological Institute – Athens, Greece*
Marek Miszczyk	*Institute of Plant Protection, National Research Institute – Sośnicowice, Poland*
Isabelle Monisse	*Laboratory of safety Food Agency – Wandre, Belgium*
Olga Nováková	*UKZUZ National Reference Laboratory – Brno, Czech Republic*
Vasilav Penev	*NSPP Central Laboratory for Chemical Testing and Control – Sofia, Bulgaria*
Olivier Pigeon	*Agricolture and Natural Environment Department (D3) – Gembloux, Belgium*
Andrew Plumb	*Fera Science Ltd – York, United Kingdom*

ARPA: Agenzia Regionale per la Protezione Ambientale

GLOSSARY

Active ingredient. An Active Ingredient (AI) is the ingredient in a pharmaceutical drug or plant-health drug that is biologically active. Some products may contain more than one active ingredient.

Analyte. An analyte, component, or chemical species is a substance or chemical constituent that is of interest in an analytical procedure.

CAS number. A CAS Registry Number, also referred to as CASRN or CAS Number, is a unique numerical identifier assigned by the Chemical Abstracts Service (CAS) to every chemical substance described in the open scientific literature (currently including all substances described from 1957 through the present, plus some substances from the early or mid-1900s) including organic and inorganic compounds, minerals, isotopes, alloys and no structural materials (UVCBs, of unknown, variable composition, or biological origin). The registry maintained by CAS is an authoritative collection of disclosed chemical substance information. It currently identifies more than 141 million unique organic and inorganic substances and 67 million protein and DNA sequences, plus additional information about each substance. It is updated with around 15,000 additional new substances daily.

Chemical formula. A chemical formula is a way that chemists describe a molecule. The formula says what atoms, and how many of each type, are in the molecule. Sometimes the formula shows how the atoms are linked, and sometimes the formula shows how the atoms are arranged in space. The letter shows what chemical element each atom is.[1] The subscript shows the number of each type of atom.

% CV. The coefficient of variation (CV) is defined as the ratio of the standard deviation σ to the mean μ multiplied 100: $CV = (\sigma / \mu) \times 100$.

E isomer. is the IUPAC convention of a molecular configuration, if the two groups of higher priority are on opposite sides of the double bond, the bond is assigned the configuration E (from the German word for "opposite" *entgegen*).

Grand Average. The grand mean or average is the mean of the means of several subsamples, as long as the subsamples have the same number of data points. For example, consider several lots, each containing several items. The items from each lot are sampled for a measure of some variable and the means of the measurements from each lot are computed. The mean of the measures from each lot constitutes the subsample mean. The mean of these subsample means is then the grand mean.

Homogeneity. Homogeneity and heterogeneity are concepts often used in the sciences and statistics relating to the uniformity in a substance or organism. A material or image that is homogeneous is uniform in composition or character (i.e., colour, shape, size, weight, height, distribution, texture, language, income, disease, temperature, radioactivity, architectural design, etc.); one that is heterogeneous is distinctly non uniform in one of these qualities.

Internal Standard. An internal standard in analytical chemistry is a chemical substance that is added in a constant amount to samples, the blank and calibration standards in a chemical analysis. This substance can then be used for calibration by plotting the ratio of the analyte signal to the internal standard signal as a function of the analyte concentration of the standards. This is done to correct for the loss of analyte during sample preparation or sample inlet. The internal standard is a compound that is very similar, but not identical to the chemical species of interest in the samples, as the effects of sample preparation should, relative to the amount of each species, be the same for the signal from the internal standard as for the signal(s) from the species of interest in the ideal case.

MAD. In statistics, the Median Absolute Deviation (MAD) is a robust measure of the variability of a univariate sample of quantitative data. MAD = median of ($|X_i$ – median (Xi) $|_{i=1,2…n}$).

Median. The median is the value separating the higher half of a data sample, a population, or a probability distribution, from the lower half. For a data set, it may be thought of as the "middle" value. For a continuous probability distribution, the median is the value such that a number is equally likely to fall above or below it. The median is a commonly used measure of the properties of a data set in statistics and probability theory. The basic advantage of the median in describing data compared to the mean (often simply described as the "average") is that it is not skewed so much by extremely large or small values, and so it may give a better idea of a "typical" value. Because of this, the median is of central importance in robust statistics.

Modified z-score. The z-score of an observation is defined as $Zi = (X - \mu) / \sigma$, where X is a sample, μ the sample mean and σ the standard deviation. In other words, data is given in units of how many standard deviations it is from the mean. Although it is common practice to use z-scores to identify possible outliers, this can be misleading in particularly for small sample sizes, so is better to use the modified z-score:

$$Zi = 0.6745 \times {}^{(Xi - median)} / MAD$$

The modified z-scores with an absolute value of greater or lower than 3.5 be labelled as an outlier.

Outlier. An outlier is an observation that appears to deviate markedly from other observations in the sample. Identify potential outliers is important because it may indicate a bad data. For example, the data may have been coded incorrectly or an experiment may not have been run correctly. If it can be determined that an outlying point is in fact erroneous, then the outlying value should be deleted from the analysis (or corrected if possible). If it is not possible to simply delete the outlying observation, the use of robust statistical techniques may be considered.

Reference Method. A reference method is an analytic procedure sufficiently free of random or systemic errors to make it useful for validating proposed new analytic procedures for the same analyte. This method has to be accuracy of a definitive method already certified demonstrated through direct comparison and must use primary reference material (standards, glasses, instruments). An in-house method it means that the method is not certified and made with the laboratory's instruments and techniques. The CIPAC methods is an analytical method make following CIPAC's instructions as the Manufacturer's method is make with the Manufacturer's instructions.

SD. The standard deviation (SD, also represented by the Greek letter sigma σ or the Latin letter s) is a measure that is used to quantify the amount of variation or dispersion of a set of data values. A low standard deviation indicates that the data points tend to be close to the mean of the set, while a high standard deviation indicates that the data points are spread out over a wider range of values.

Stability. The stability is a molecular characteristic of a chemical or compound; is the tendency of a material to resist change or decomposition in its natural environment or when exposed to air, heat, light, pressure or other natural conditions or due to internal reaction.

Z isomer. is the IUPAC convention of a molecular configuration, if the two groups of higher priority are on the same side of the double bond, the bond is assigned the configuration Z (from the German word for "together" *zusammen*).

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Roma, novembre 2019