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Results of the proficiency test on plant protection products in 2024

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AMBIENTE E SALUTE

ISTITUTO SUPERIORE DI SANITÀ

Results of the proficiency test on plant protection products in 2024

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Rapporti ISTISAN 25/19

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Angela Santilio, Roberto Cammarata, Silvana Girolimetti
2025, v, 42 p, Rapporti ISTISAN 25/19

In 2024, the seventh Proficiency Test (PT) on plant protection products available on the Italian market was organized. The aim was to find out the quantity of active ingredients in the different formulations of the plant protection products. Seven Italian laboratories and thirteen European laboratories that routinely deal with pesticides were invited to participate. Participation is voluntary and all laboratories have joined. Most of the laboratories obtained data with acceptable z-score values within the limits $-3.5 \leq Z \leq +3.5$.

Key words: Proficiency test; Plant protection products; Bentazone; Boscalid; Fluroxypyr

Istituto Superiore di Sanità
Risultati dell'esercizio interlaboratorio sui prodotti fitosanitari nel 2024.
Angela Santilio, Roberto Cammarata, Silvana Girolimetti
2025, v, 42 p, Rapporti ISTISAN 25/19 (in inglese)

Nel 2024 è stato organizzato il settimo esercizio inter-laboratorio 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 7 laboratori italiani preposti al controllo dei prodotti fitosanitari e 13 laboratori europei interessati ai controlli sui prodotti fitosanitari. La partecipazione è su base volontaria e tutti i laboratori invitati hanno aderito. La maggior parte dei laboratori hanno ottenuto risultati con valori di *z-score* entro i limiti definiti $-3{,}5 \leq Z \leq +3{,}5$.

Parole chiave: Esercizio inter-laboratorio; Prodotti fitosanitari; Bentazone; Boscalid; Fluroxypyr

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ABBREVIATIONS

AAPCO	Association of American Pesticide Control Officials
AFSCA	Agence fédérale pour la sécurité de la chaîne alimentaire (Federal Agency for the Safety of the Food Chain)
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council
CS	Capsule Suspension
CV	Coefficient of Variation
DAD	Diode Array Detector
FID	Flame Ionisation Detector
GC	Gas Chromatography
HRMS	High Resolution Mass Spectrometry
HPLC	High Performance Liquid Chromatography
ISO	International Organization for Standardization
ITPT	Italian Proficiency Test
LC	Liquid Chromatography
MAD	Median absolute deviation
MS	Mass Spectrometry
N/A	Not Available
PDA	PhotoDiode Array
PTFE	Polytetrafluoroethylene
PPP	Plant Protection Product
PPP01	Plant Protection Product number 1
PPP02	Plant Protection Product number 2
PPP03	Plant Protection Product number 3
PRSD	Predicted Relative Standard Deviation
PT	Proficiency Test
RSD	Relative Standard Deviation
SC	Suspension Concentrate
SD	Standard Deviation
SL	Soluble Concentrate
UV	UltraViolet
VIS	Visible
VWD	Variable Wavelength Detector
z-score	Standard Score

Symbols

σ_{PT}	standard deviation for proficiency test
T-test	statistic test of Student's t distribution

PREFACE

The European legislation on Plant Protection Products (PPPs) – Regulation (EC) 1107/2009) – 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 which they might consist of.

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 improving agricultural production.

In addition, the Regulation (EU) 2017/625 establishes 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 instruments to reach a high-quality standard and performance is the participation in the interlaboratory test (Proficiency Test, PT) to demonstrate that the analytical data obtained from laboratories are reliable. For this reason, it is important to organize PTs for the active ingredient content for the official laboratories.

As the national monitoring programs are in comply with the European monitoring programs, it is useful to enlarge the invitation to European Member State laboratories that work on this issue.

This activity was planned in the framework of the collaboration (CUP I85E24000440005) with the Ministry of Health and the Istituto Superiore di Sanità (ISS, the National Institute of Health in Italy).

As defined in the collaboration agreement, the Department of Environment and Health of the ISS organised a PT for the year 2024 for the detection of active ingredient in PPPs available on the Italian market.

The laboratory provider is accredited according to the ISO/IEC 17025 but is not accredited according to the ISO/IEC 17043.

INTRODUCTION

The 7th Italian PT on PPPs (later indicated as ITPT2024) was organized between November 2023 and April 2024.

The announcement letter (Appendix A) sent to the laboratories on 7th November 2023, according to the calendar. The laboratories sent confirmation of participation by email.

Seven Italian laboratories and 13 European laboratories received the invitation.

All relevant Italian laboratories and European Member State laboratories participated in the ITPT2024.

In January, three different commercial products containing three active ingredients (Fluroxypyr meptyl 292 g/kg; Boscalid 500 g/kg; Bentazone 870 g/kg) were shipped to the laboratories.

Each participant received the sample bottles.

The relevant documents, such as Safety Disposable Sheets (SDS), technical instructions and the result report form were sent by e-mail. It was requested to determine the content of active ingredient using a routine analytical method applied in each participant's laboratory.

The participants were asked to report the measurement results in three significant figures in the provided result form. Also, the laboratories gave technical information on their methods, such as extractant, sample preparation, injection volume, the column used, column temperature and detector used.

The deadline of the test results submission was in April 2024.

1. PROFICIENCY TEST ON PLANT PROTECTION PRODUCTS

1.1. Test materials

The test materials of the ITPT2024 consisted of three PPPs obtained from manufacturer and available from Italian market. The product types are: Water Dispersible Granule (WG), Water soluble granule (SG) and Emulsifiable Concentrate (EC) at a declared concentration reported in Table 1.

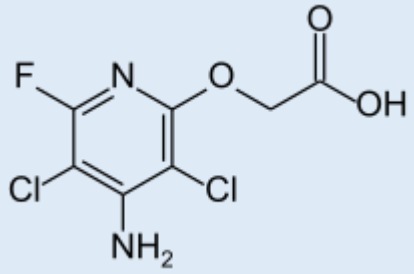
Table 1. Test materials of ITPT2024

Check Sample N.	Product description	Active ingredient	Declared level g/kg
PPP01	Emulsifiable Concentrate	Fluroxypyr as ester (Fluroxypyr as acid)	292 (203)
PPP02	Water Dispersible Granule	Boscalid	500
PPP03	Water Soluble Granule	Bentazone	870

For the preparation of the subsamples to send each laboratory, the PPPs were mixed mechanically and divided in 20 samples, for a total of 60 plastic containers sealed and stored at ambient temperature before the shipment to the participants. Each laboratory received three samples. Nothing added to our samples.

1.2. Description of the active substances in the PPPs

1.2.1. Fluroxypyr meptyl



Common name Fluroxypyr meptyl

IUPAC name

[(4-Amino-3,5-dichloro-6-fluoropyridin-2-yl)oxy]acetic acid

(RS)-1-Methylheptyl(4-amino-3,5-dichloro-6-fluoro-2 pyridyloxy)acetate

Structure Formula $C_7H_5Cl_2FN_2O_3$ acid

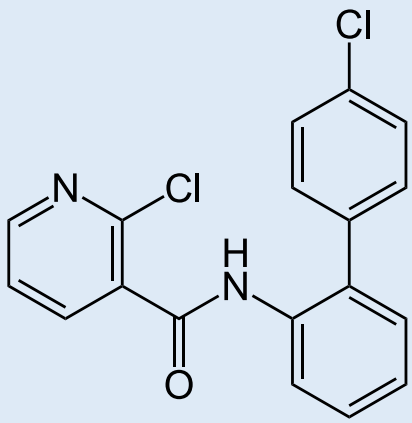
$C_{15}H_{21}Cl_2FN_2O_3$ ester

CAS number 69377-81-7 acid

81406-37-3 ester

Fluroxypyr is the ISO common name for 4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic acid (IUPAC). The meptyl ester, a variant of fluroxypyr, is used in the formulated product. Fluroxypyr is an herbicide in the class of synthetic auxins. It is used to control broadleaf weeds and woody brush.

1.2.2. Boscalid



Common name Boscalid

IUPAC name
(2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl)pyridine-3-carboxamide

Structure formula $C_{18}H_{12}Cl_2N_2O$

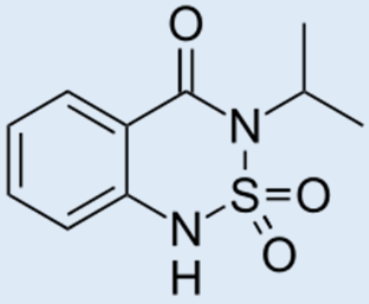
CAS number 188425-85-6

Boscalid is a broad spectrum fungicide used in agriculture to protect crops from fungal diseases. It was first marketed by BASF in 2002 using their brand name Endura. The compound is an biphenyl amide derived inhibitor of succinate dehydrogenase.

Inhibition of succinate dehydrogenase, the complex II in the mitochondrial respiration chain, has been known as a fungicidal mechanism of action since the first examples were marketed in the 1960s. The first compound in this class was carboxin, which had a narrow spectrum of useful biological activity, mainly on basidiomycetes and was used as a seed treatment. Many companies made analogues with the aim of expanding the range of species controlled and boscalid was successful in doing so.

Boscalid has fungicidal effects against a wide range of crop pests. These include Alternaria, grey mold (*Botrytis cinerea*), white mold (*Sclerotinia sclerotiorum*), and powdery mildew (*Uncinula necator*). As a result, it has use in crops including fruits, soybeans and vegetables.

1.2.3. Bentazone



Common name Bentazone

IUPAC name
3-isopropyl-1H-2,1,3-benzothiadiazin-4(3H)-one 2,2-dioxide

Structure formula $C_{10}H_{12}N_2O_3S$

CAS number 25057-89-0

Bentazone is benzothiadiazinone with a molecular weight of 240.3 g/mol.

It is herbicide, absorbed mainly by foliage, with very little translocation, but also absorbed by the roots, with translocation acroèetally in ht exylem.

Bentazone is used as contact herbicide. It is a selective herbicide as it only damages plants unable to metabolize the chemical. It is usually applied through contact spraying on food crops to control the spread of weeds occurring amongst food crops.

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.

For the determination of the homogeneity and stability test, the organiser used the CIPAC MT 366 method for Bentazone, CIPAC MT 673 for Boscalid and manufacturer's method for Fluroxypyr meptyl.

1.3.1. Bentazone analytical method

For determination of Bentazone, weight a quantity of sample corresponding to 70 mg of Bentazone into a 100-mL volumetric flask and add 4 mL of MetOH and 6 mL of sodium acetate buffer 0.074 N. Add 50 mL of mobile phase (MetOH/sodium acetate buffer, 40:60 v/v), mix well and fill up to volume 100 mL with mobile phase. Mix well and filter 1 mL on 0.45 µm PTFE filter before injection.

The determination was performed using HPLC/DAD at 340 nm, a Zorbax SB C18 column 250 x 4.6 mm; 5 µm was used; flow rate was 1 mL/min; column temperature: 25°C; mobile phase: MetOH/sodium acetate buffer 0.075N (40:60, v/v).

1.3.2. Boscalid analytical method

For determination of Boscalid, weight a quantity of sample corresponding to 100 mg of Boscalid into a 100-mL volumetric flask and a volume of 10 mL of water was added. The solution was mixed and added 50 mL of acetonitrile. Then, sonicate for 5 minutes and after cooling, fill up to volume with water and mix well. 10 mL of this solution was diluted in a volumetric flask (50 mL) and mark to volume with acetonitrile. One mL of this solution was filtered on 0.2 µm PTFE filter before injection.

The determination was performed using HPLC/DAD at 260 nm, a Allure C18 column 250 x 4.6 mm; 5 µm was used; flow rate was 1 mL/min; column temperature: 25°C; mobile phase: water/acetonitrile/ammonium acetate buffer in gradient way.

1.3.3. Fluroxypyr meptyl analytical method

For determination of Fluroxypyr meptyl, weight a quantity of sample corresponding to 150 mg of Fluroxypyr meptyl. Dilute with 90 mL acetonitrile, sonicate for 4 minutes and mix allow to cool to room temperature and fill up to the mark with acetonitrile (100 mL). Filter on 0.45 mm PTFE (polytetrafluoroethylene) before injection.

The determination was performed using High Performance Liquid Chromatography Coupled Diode Array detector (HPLC/DAD) at 254 nm, a Zorbax SB C18 column 250 x 4.6 mm; 5 µm was used; flow rate was 1 mL/min; column temperature: 25°C; mobile phase: acetonitrile/H_2O acidify with H_3PO_4 pH=3 in isocratic mode.

1.3.4. 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 statistically significant differences between PT items were 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 and the samples are homogeneous.

The results are shown in Table 2 for all compounds and the concentrations are in g/kg.

Table 2. Homogeneity results of the PT samples (ITPT2024)

Sample ID	Fluroxypyr-meptyl (g/kg)		Boscalid (g/kg)		Bentazone (g/kg)	
	a	b	a	b	a	b
#1	314.9	314.9	495.1	494.2	876.7	878.3
#2	310.9	297.7	494.8	492.9	871.9	874.6
#3	304.7	298.4	497.2	494.3	883.3	883.5
#4	308.6	308.6	499.8	497.5	898.8	895.2
#5	305.5	302.8	498.9	496.2	886.2	879.8
#6	312.6	311.3	503.7	492.0	893.0	887.9
#7	317.9	317.7	509.3	496.3	880.2	879.2
#8	309.9	308.2	505.3	500.4	887.4	886.9
#9	309.7	309.9	515.3	505.9	870.9	882.8
#10	303.2	304.4	493.8	496.3	872.1	877.1
Mean	309.8	307.4	501.3	496.6	882.0	882.5
SD	4.6	6.6	7.1	4.0	9.5	6.1
t**	0.9443		1.8351		0.1326	
P***	0.3575		0.0831		0.8959	
Homogeneity	YES		YES		YES	

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

For Fluroxypyr meptyl, the data obtained confirm that the sample is homogeneous but the mean concentration obtained in two days were higher than the label declared. The label content declared is 292 g/kg and the tolerance is ±5%, the range concentration is 277.4-306.6 g/kg. However, we decide to use this product for the PT.

As concern, Boscalid and Bentazone the result obtained confirm that the products are homogeneous and the active substance contents are according to the label conctent declared.

For Boscalid the label declared concentration is 500 g/kg and the tollerance is ±5%, the range concentration is 475-525 g/kg.

The label declared content for Bentazone is 870 g/kg, the tollerance is ±25 g/kg and the range concentration is 845-895 g/kg.

1.3.5. 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 in January 2024;
- *Day 2*: at the deadline for reporting results in April 2024.

Stability test was judged acceptable as the percentage difference of concentration, for each active substance was found less than 10%,

Table 3 shows the stability data of the ITPT2024.

Table 3. Summary of stability data in g/kg (ITPT2024)

Active ingredient	January	April	Concentration
Fluroxypyr-meptyl	312.4	313.4	292
Boscalid	497.7	497.6	500
Bentazone	882.9	886.6	870

Tables 4, 5, and 6 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 are stable.

Table 4. FLUROXYPYR MEPTYL: results of stability test (ITPT2024)

Parameter	January				April			
	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	307.1	316.7	312.1	315.4	311.3	317.7	312.2	315.8
Sample 2	309.3	313.8	307.7	316.8	305.4	317.4	310.6	316.8
Mean	311.7		313.0		313.0		313.9	
SD	4.3		4.0		5.8		2.9	
Mean of 2 days	312.4				313.4			
Standard Deviation of 2 days	0.9				0.6			
Deviation (ref 1st Analysis)/ [(M2-M1)/M1]*100	-0.33							
Deviation (ref to declared label g/kg)/ [(SM-292)/292]*100	7.16							
Stability Mean	312.9		Declared Label g/kg		292			
Stability Standard Deviation	0.7		CV %		0.23			

Regarding Fluroxypyr meptyl, we noted that the deviation referred to label declared content is 7.16%. Based on the European Regulation (EU) n.1107/2009, the tolerance for the product with content >250 up to 500 g/kg is ±5%. For Fluroxypyr meptyl, the tolerance interval is 277.4-306.6 g/kg as a consequence we noted that the Fluroxypyr content is more than the tolerance limit. We confirm the result obtained in the homogeneity test.

For Boscalid and Bentazone, the results confirm the stability of the products and the agreement to the declared label content.

Table 5. BOSCALID: results of stability test (ITPT2024)

Parameter	January				April			
	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	497.2	495.4	496.6	496.3	496.6	496.3	490.5	499.1
Sample 2	499.5	500.6	498.0	498.2	498.0	498.2	506.0	496.0
Mean	498.2		497.3		497.3		497.9	
SD	2.3		1.0		1.0		6.5	
Mean of 2 days	497.7				497.6			
Standard Deviation of 2 days	0.6				0.4			
Deviation (ref 1st Analysis)/ [(M2-M1)/M1]*100	-0.03							
Deviation (ref to declared label g/kg)/ [(SM-500)/500]*100	-0.47							
Stability Mean	497.7		Declared Label g/kg		500			
Stability Standard Deviation	0.1		CV %		0.02			

Table 6. BENTAZONE: results of stability test (ITPT2024)

Parameter	January				April			
	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	874.9	876.6	884.0	882.7	892.0	887.0	879.9	887.1
Sample 2	874.2	879.2	896.5	895.2	885.9	890.7	887.1	882.7
Mean	876.2		889.6		888.9		884.2	
SD	2.2		7.3		2.9		3.5	
Mean of 2 days	882.9				886.6			
Standard Deviation of 2 days	9.5				3.3			
Deviation (ref 1st Analysis)/ [(M2-M1)/M1]*100	0.41							
Deviation (ref to declared label g/kg)/ [(SM-300)/300]*100	1.69							
Stability Mean	884.7		Declared Label g/kg		870			
Stability Standard Deviation	2.6		CV %		0.29			

1.4. Distribution of the samples and instructions for the participants

Three plastic transparent containers were filled. 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 made 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 participants on 15th January 2024.

The deadline for results was 30th of April 2024.

The final report was dispatched to all participants at the end of September 2024.

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 the modified z-score.

A Horwitz ratio (HorRat) has been calculated. The HorRat is a normalized performance parameter indicating the acceptability of analytical methods respect to among-laboratory precision (reproducibility). It illustrates the deviation or agreement of an observed interlaboratory reproducibility with typical values. In this PT, the HorRat for the laboratories was calculated for each substance.

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.

1.5.3. Calculation of Horwitz ratio

A HorRat can be calculated using RSD (Relative Standard Deviation), which is defined as follow:

$$HorRat = RSDr/PRSDr$$

where RSDr is the RSD among laboratories and PRSDr is the predicted standard deviation from Horwitz equation:

$$PRSDr(\%) = 2C^{-0.15}$$

where C is the concentration found expressed as a mass fraction,

The empirical acceptable HorRat value is ranged between 0.5-2.0.

1.5.4. Presentation of data

Data is presented graphically in two ways:

- A plot of modified z-scores.
- 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.

2. ANALYSIS OF THE SUBSTANCES

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

2.1. Fluroxypyr

For the active substance Fluroxypyr, 20 boxes were sent to all laboratories, in particular 7 to Italian's Laboratories and 13 to European Laboratories outside Italy. We received 16 participation results, twelve laboratories used for the analysis an HPLC instrument with a UV or PDA Detector and 4 used a Gas Chromatography (GC) with Flame Ionization Detector (FID).

To carry out this analysis, 12 laboratories applied an in-house method and 4 the manufacturer's method, as is shown in Table 7.

Table 7. FLUROXYPYR: methods applied for analysis (ITPT2024)

Laboratories	In-house	CIPAC	Manufacturer's
Number	12	0	4

For Fluroxypyr, some laboratories gave the results as acid and others as ester. We calculated the z-score separately and considering the median values as reference value.

For Fluroxypyr, 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 with the possibility of outlying data points without having to remove them, so the median and the standard deviation were used.

For Fluroxypyr as acid, the results obtained indicate that for all laboratories the z-score values are within the acceptability range, as reported in Figure 1.

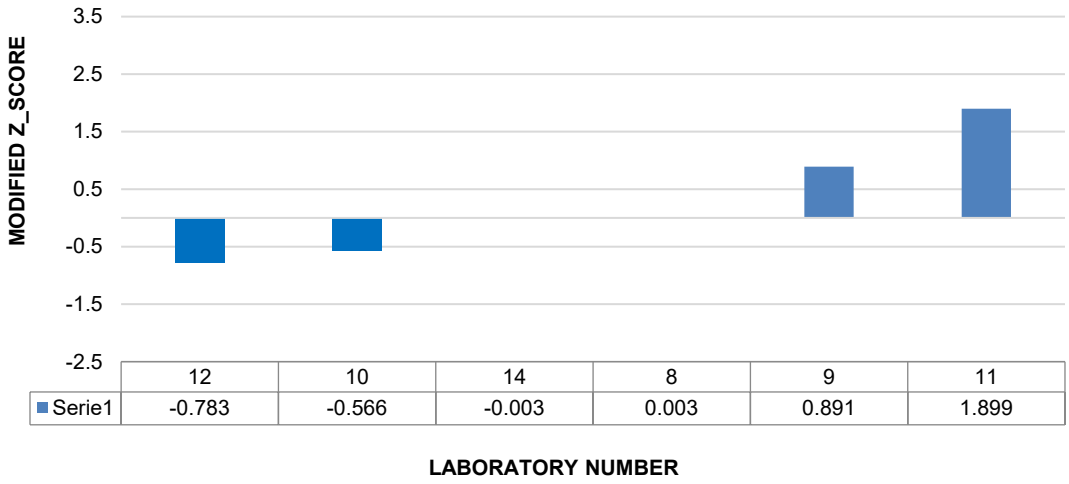


Figure 1. FLUROXYPYR ACID: modified z-scores (ITPT2024)

For Fluroxypyr acid, the number of laboratories is very low; nevertheless, the sample is homogeneous and stable on the test of Jarque Berà. Considering the small sample size and the adjustment to the median of the Horwitz/Thompson data, the data are still consistent with z-score, but the Horwitz limits, considering the equity on the median of the base data, appear internal to those of the MAD/MADe, which entails the acceptance of data.

Figure 2 shows the distribution of the data respect to the median value and the range for Horwitz/Thompson and MAD/MADe.

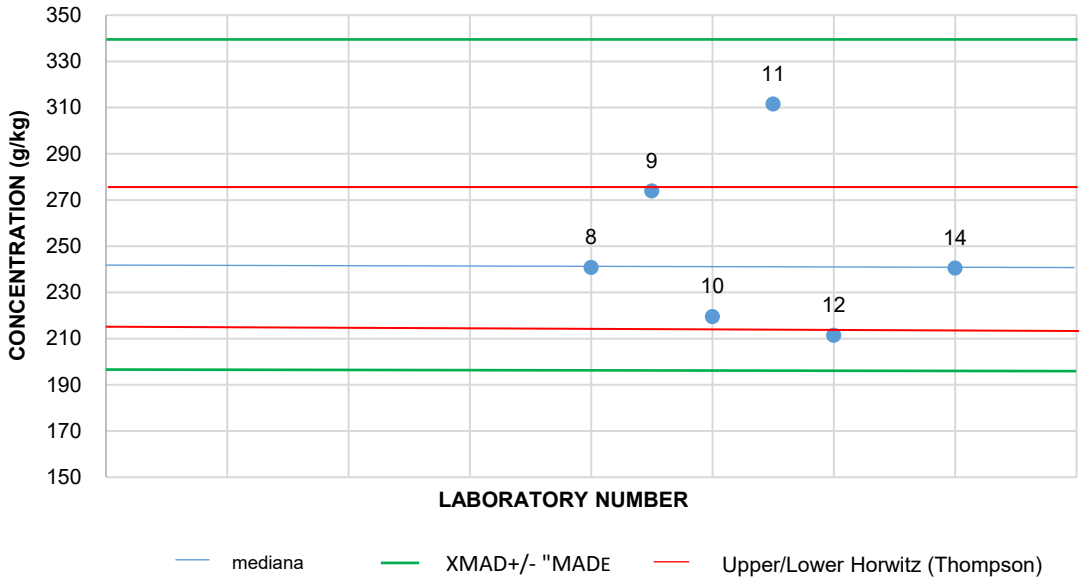


Figure 2. FLUROXYPYR ACID: distribution data, median value, Horwitz/Thompson range, MAD/MADe range (ITPT2024)

Figure 3 shows the z-score values for all laboratories that analysed Fluroxypyr as ester. Most of laboratories obtained z-score value acceptable except three laboratories that are out of the acceptability range.

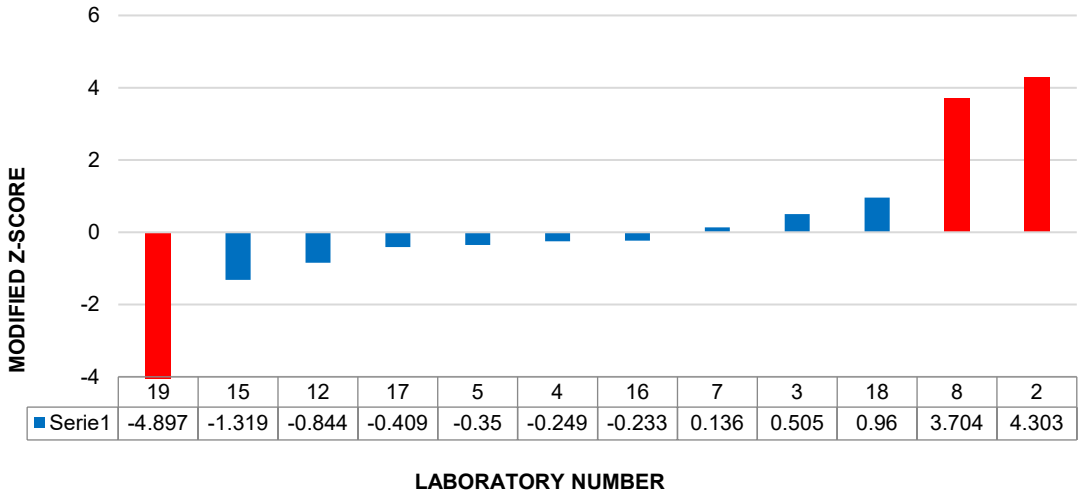


Figure 3. FLUROXYPYR ESTER: modified z-scores (ITPT2024)

For Fluroxypyr as ester, the sample is homogeneous and stable on the test of Jarque Berà. The data are consistent with z-score.

Figure 4 shows the distribution of the data respect to the median value and the range for Horwitz/Thompson and MAD/MADe.

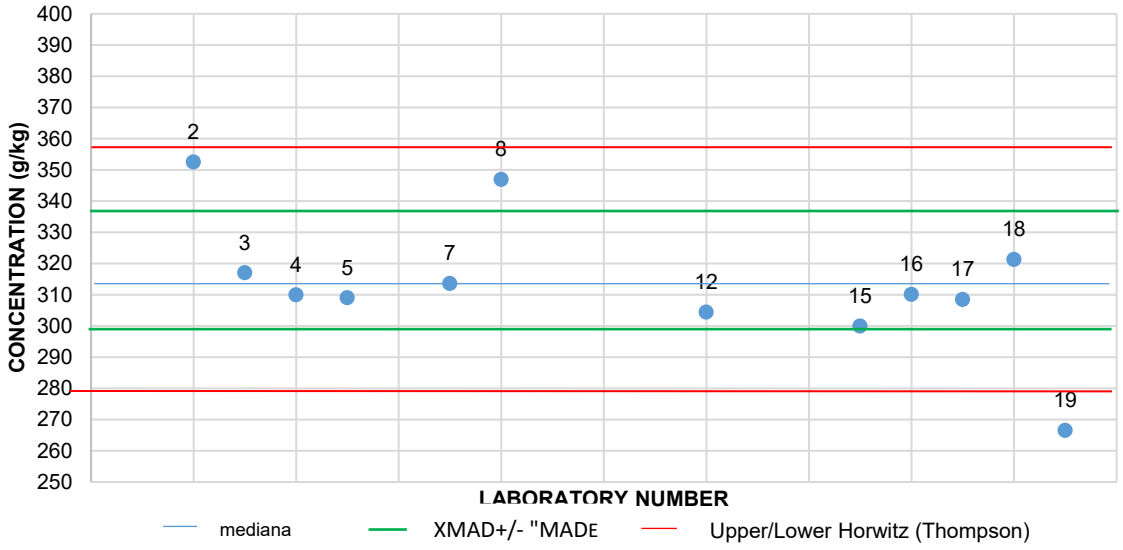


Figure 4. FLUROXYPYR ESTER: distribution data, median value, Horwitz/Thompson range, MAD/MADe range (ITPT2024)

In addition, we converted the results of the fluroxypyr as acid in ester with the following formula

$$Cester = (Cacid\ x\ MWester)/MWacid$$

where

Cester is the concentration as ester (g/kg)
Cacid is concentration as acid (g/kg)
MWacid is molecular weight of acid (255.03)
MWester is molecular weight of ester (367.24)

we obtained the z-score value reported in Table 8.

Table 8 shows the z-score values calculated for all laboratories as Fluroxypyr meptyl. It is noted that for all laboratories the z-score values are acceptable except for two laboratories for which the z-score values are out of the acceptability range.
After this conversion and recalculation, we observed for laboratories 2, 8, and 19 z-score values are acceptable while the laboratories 9 and 11 obtained the z-score values out of the acceptability range. The median value used to calculate the z-score value influence the acceptability of the results.

Table 8. FLUROXYPYR: z-score values calculated as fluroxypyr meptyl for all laboratories (ITPT2024)

Laboratories	z-score value as Fluroxypyr-meptyl (after conversion)	z-score value as Fluroxypyr-meptyl	z-score value as Fluroxypyr-acid
2	**2.59**	**4.30**	
3	0.14	0.51	
4	-0.35	-0.25	
5	-0.41	-0.35	
7	-0.10	0.14	
8	**2.21**	**3.70**	0.00
9	**5.49**	**--**	**0.89**
10	0.08	--	-0.57
11	**9.23**	**--**	**1.90**
12	-0.73	-0.84	-0.78
14	2.17	--	0.00
15	-1.04	-1.32	
16	-0.34	-0.23	
17	-0.45	-0.41	
18	0.44	0.96	
19	**-3.35**	**-4.90**	

The HorRat value calculated was 1.69 as ester that indicates good acceptability of the chemical methods used with respect to precision. Moreover, the HorRat value calculated as acid was 4.00 indicates inhomogeneity of the test samples, or an unsatisfactory method.

2.2. Boscalid

For the substance Boscalid 20 boxes were sent to laboratories, in particular 7 to Italian's Laboratories and 13 to European Laboratories outside Italy. We received 20 participation results. The analysis was performed using LC instrument for 17 laboratories with UV or PDA Detector and one decide to use the GC with FID, and 2 laboratories used Orbitrap mass spectrometry. Fourteen laboratories chose to use an in-house method, four CIPAC method and 2 laboratories used manufacturer's method, as is showed in Table 9. All the methods gave appreciable data.

Table 9. BOSCALID: methods applied for analysis (ITPT2024)

Laboratories	In-house	CIPAC	Manufacturer's
Number	14	4	2

Boscalid, as for the Fluroxypyr mentioned before, on the collected data a statistical evaluation based on a robust estimator (median) instead the mean was applied. The purpose of this choice was to handle possible outlier data points instead of removing them, so it was used the median and the standard deviation, Figure 5 shows the lab's values of the modified z-score.

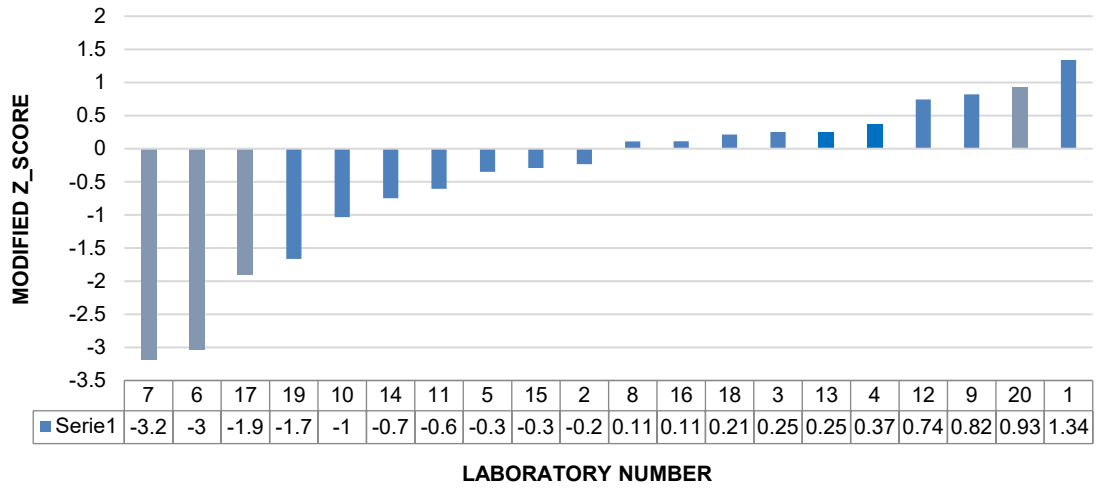


Figure 5. BOSCALID: modified z-scores (ITPT2024)

The results obtained are valuable data, in fact all of them are inside the z-score range of $-3.5 \leq Z \leq +3.5$.

The HorRat value calculated was 2.0 that indicates good acceptability of the chemical methods used with respect to precision.

For Boscalid, the sample is homogeneous and stable on the test of Jarque Berà. The data are consistent with z-score.

Figure 6 shows the distribution of the data respect to the median value and the range for Horwitz/Thompson and MAD/MADe.

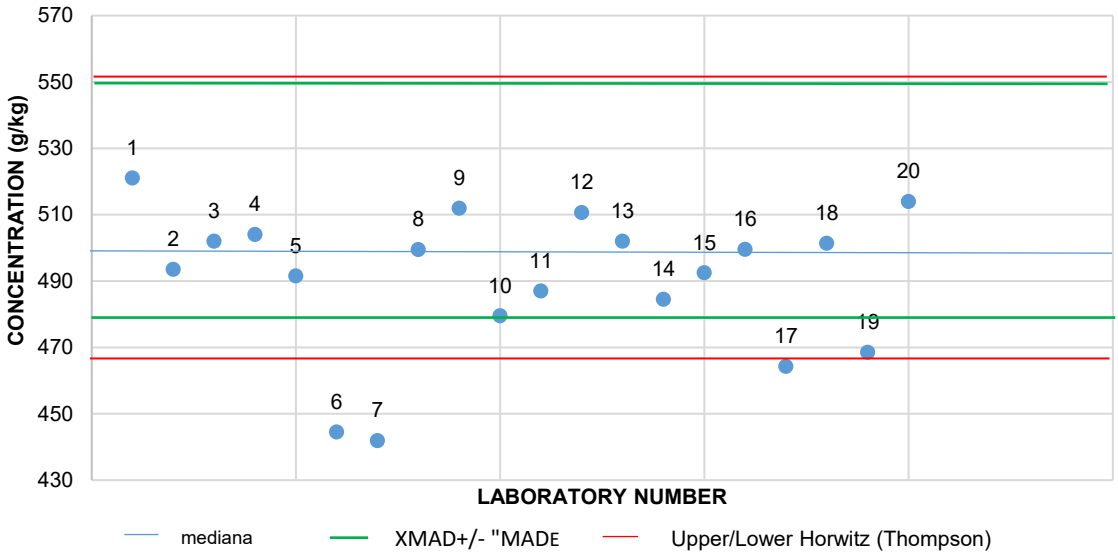


Figure 6. BOSCALID: distribution data, median value, Horwitz/Thompson range, MAD/MADe range (ITPT2024)

2.3. Bentazone

Regarding the active substance Bentazone, 20 boxes were sent to all over the world, in particular 7 to Italian's Laboratories and 13 to European Laboratories outside Italy. We received 18 participation results. 17 laboratories used for the analysis an LC instrument with a UV or PDA Detector and 1 laboratory used the Orbitrap mass spectrometry as detector. It is interesting to note that 12 laboratories chose to use an in-house method, 5 laboratories choose to use CIPAC methods, one applied a manufacturer's method, as is showed in Table 10. At the same time, all the methods gave appreciable data.

Table 10. BENTAZONE: methods applied for analysis (ITPT2024)

Laboratories	In-house	CIPAC	Manufacturer's
Number	12	5	1

On the collected data, a statistical evaluation based on a robust estimator (median) instead the mean was applied. 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 laudable data, in fact all of them are inside the modified z-score range of $-3.5 \leq Z \leq +3.5$.

The HorRat value calculated was 1.2 that indicates good acceptability of the chemical methods used with respect to precision.

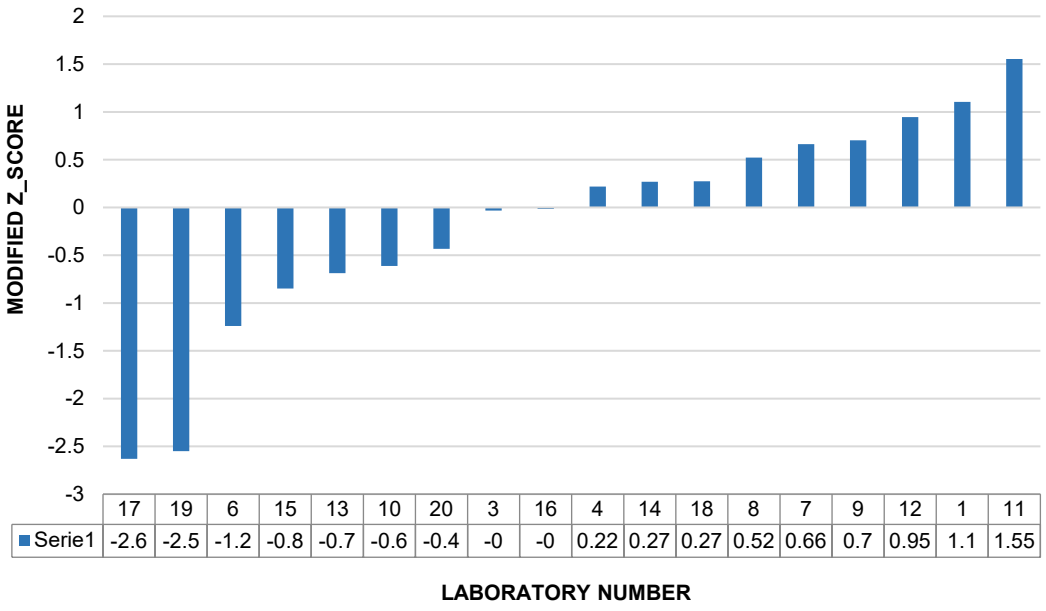


Figure 7. BENTAZONE: modified z-scores (ITPT2024)

For Bentazone, the sample is homogeneous and stable on the test of Jarque Berà. The data are consistent with z-score.

Figure 8 shows the distribution of the data respect to the median value and the range for Horwitz/Thompson and MAD/MADe.

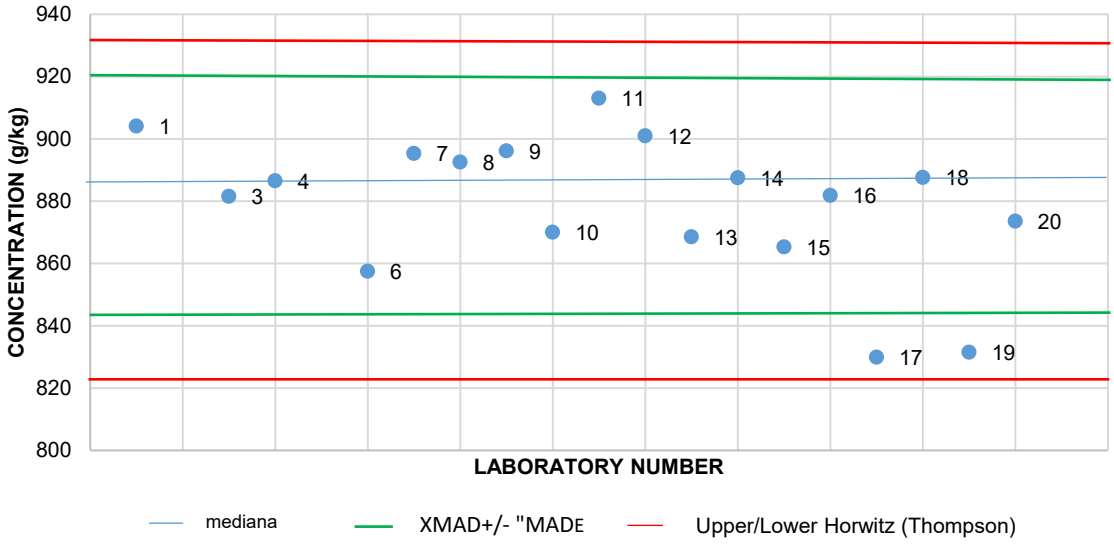


Figure 8. BENTAZONE: distribution data, median value, Horwitz/Thompson range, MAD/MADe range (ITPT2024)

3. RESULTS

The result of the 7th PT (ITPT2024) can be regarded as satisfactory.

The exercise received good interest from participating laboratories.

The participation of the Italian and European laboratories was good.

For Italy, seven laboratories participated so distributed: three of the north, three in central and one in the south of the Country. The European laboratories were thirteen, excluding Italy, distributed throughout eight in Nord Europe, three in Central Europe and 2 in the South Europe. For Belgium, 2 laboratories participated and one laboratory for the other countries.

For the analysis of Fluroxypyr, 75% of the laboratories used the in-house method and 25% used manufacturer's method.

As concern Boscalid, 70% of the laboratories used in-house methods, 20% CIPAC method and 10% manufacturer's method.

Finally, for Bentazone, 67% of the laboratories used in-house methods, 28% CIPAC method and 5% manufacturer's method.

Most of the laboratories used LC and only few laboratories used GC technique. For fluroxypyr as ester we observed 0.25% failing results (Table 10).

Table 11. Summary of participation per active ingredient (ITPT2024)

ID Sample	Product description	Active ingredient	Participants (n.)	Labs using GC (n.)	Labs using LC (n.)	Failing results[1](%)
PPP01	Emulsifiable Concentrate	Fluroxypyr as acid Fluroxypyr as ester	16	4	12	0.25
PPP02	Water dispersible granule	Boscalid	20	2	18	0
PPP03	Water soluble granule	Bentazone	18	0	18	0

[1] Where failing indicates a mean assay result outside the modified z-score defined acceptable limits.

For each substance, the HorRat value calculated indicates the good acceptability of the chemical methods used with respect to the precision. The HorRat value for Fluroxypyr calculated as acid was 4.00 indicates inhomogeneity of the test samples, or an unsatisfactory method.

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

The performance of the laboratories in terms of modified z-score was satisfactory for almost all participants for all substances. For all active substance, there are not outlier values.

Table 12. Summary of lab results per active ingredient, including outliers (ITPT2024)

ID Sample	Analyte (Label claim)	Minimum result (g/kg)	Maximum result (g/kg)	Grand Average (g/kg)	Grand %CV
PPP01	Fluroxypyr as ester (292g/kg)	266.5	352.5	313.1	6.7
	Fluroxypyr as acid (203g/kg)	211.4	311.5	249.6	1.5
PPP02	Boscalid (500g/kg)	441.9	521.0	490.3	4.4
PPP03	Bentazone (870g/kg)	829.9	913.0	879.1	2.5

Table 13. Summary of lab results per active ingredient, excluding outliers (ITPT2024)

ID Sample	Analyte (Label claim)	N, of outliers[1]	Average excluding outliers	%CV excluding outliers
PPP01	Fluroxypyr as ester (29 2g/kg)	3	310.40	2.05
	Fluroxypyr as acid (203 g/kg)	0	no	no
PPP02	Boscalid (500 g/kg)	0	no	no
PPP03	Bentazone (870 g/kg)	0	no	no

[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.

Based on the results, we can conclude that the PT was successful and that a satisfactory number of laboratories participated.

Tables 14, 15, 16 and 17 show details of the z-score values for each laboratory and the analytical technique used for each substance.

Tables 18, 19 and 20 report the information on analytical methods used for each substance and each laboratory.

Table 14. FLUROXYPYR as acid Sample PPP01: summary results (ITPT2024)

Lab #	Method	Two Day Average[1]	RPD[1]	Modified z score[2]	Outlier[2]
8	HPLC/UVD	240.8	-0.29	0.00	NO
9	HPLC/MS/MS	273.9	1.24	0.89	NO
10	HPLC/UV	219.5	-3.19	-0.57	NO
11	HPLC/DAD	311.5	0.32	1.90	NO
12	GC/FID	211.4	-0.19	-0.78	NO
14	HPLC/DAD	240.5	-0.42	-0.00	NO
Grand Average[3]		249.59			
Total SD		0.94			
Total Median[4]		240.63			
MAD		25.18			
MAD_E		37.34			

[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 ≤ Zi ≤ 3.5; see Glossary.
[3] Grand average, standard deviation and median.
[4] Median Absolute Deviation Robust estimation of standard deviation; see Appendix for calculations.

Table 15. FLUROXYPYR as ester Sample PPP01: summary results (ITPT2024)

Lab #	Method	Two Day Average[1]	RPD[1]	Modified z score[2]	Outlier[2]
2	GC/FID	352.50	0.85	4.30	YES
3	HPLC/UV	317.00	-	0.51	NO
4	HPLC/UV	309.95	1.13	-0.25	NO
5	HPLC/UV	309.00	1.94	-0.35	NO
7	GC/FID	313.55	0.03	0.14	NO
8	HPLC/UV	346.90	-0.52	3.70	YES
12	GC/FID	304.39	0.20	-0.84	NO
15	HPLC/UV	299.95	2.70	-1.32	NO
16	GC/FID	310.10	-1.35	-0.23	NO
17	HPLC/UV	308.45	-6.71	-0.419	NO
18	GC/FID	321.25	0.03	0.96	NO
19	HPLC/MS/MS	266.50	-0.38	-4.90	YES
Grand Average[3]		313.1			
Total SD		20.92			
Total Median[4]		312.28			
MAD		6.30			
MAD_E		9.35			

[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 ≤ Zi ≤ 3.5; see Glossary.
[3] Grand average, standard deviation and median.
[4] Median Absolute Deviation Robust estimation of standard deviation; see Appendix for calculations.

Table 16. BOSCALID Sample PPP02: summary results (ITPT2024)

Lab #	Method	Two Day Average[1]	RPD[1]	Modified z score[2]	Outlier[2]
1	HPLC/PDA	521.05	-0.56	1.34	NO
2	HPLC/DAD	493.50	2.23	-0.23	NO
3	HPLC/UV	502.00	-	0.25	NO
4	HPLC/PDA	504.00	0.79	0.37	NO
5	HPLC/UV	491.50	-2.24	-0.35	NO
6	HPLC/DAD	444.50	-0.22	-3.04	NO
7	GC/FID	441.90	-1.22	-3.18	NO
8	HPLC/DAD	499.50	0.44	0.11	NO
9	HPLC/MS/MS	511.95	-4.51	0.82	NO
10	HPLC/DAD	479.50	-0.63	-1.04	NO
11	HPLC/DAD	487.00	0.41	-0.61	NO
12	HPLC/PAD	510.60	-2.62	0.74	NO
13	HPLC/DAD	502.00	0.00	0.25	NO
14	HPLC/DAD	484.50	-1.03	-0.75	NO
15	HPLC/DAD	492.50	2.31	-0.29	NO
16	HPLC/PDA	499.55	-1.38	0.11	NO
17	HPLC/DAD	464.25	-3.68	-1.91	NO
18	HPLC/PDA	501.35	0.38	0.21	NO
19	HPLC/MS/MS	468.50	-4.48	-1.66	NO
20	HPLC/UV	513.95	-1.73	0.94	NO
Grand Average[3]			490.33		
Total SD			21.77		
Total Median[4]			497.60		
MAD			11.80		
MAD_E			17.49		

[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] Grand average, standard deviation and median.
[4] Median Absolute Deviation Robust estimation of standard deviation; see Appendix for calculations.

Table 17. BENTAZONE Sample PPP03: summary results (ITPT2024)

Lab #	Method	Two Day Average[1]	RPD[1]	Modified Z Score[2]	Outlier[2]
1	HPLC/PDA	904.10	-0.53	1.10	NO
3	HPLC/DAD	881.50	1.02	-0.03	NO
4	HPLC/PDA	886.50	-0.68	0.22	NO
6	HPLC/DAD	857.50	-2.22	-1.24	NO
7	HPLC/PDA	895.30	-0.27	0.66	NO
8	HPLC/DAD	892.50	-0.56	0.52	NO
9	HPLC/UV	896.10	0.07	0.70	NO
10	HPLC/UV	870.00	0.46	-0.61	NO
11	HPLC/DAD	913.00	-0.22	1.55	NO
12	HPLC/PDA	900.95	0.83	0.95	NO
13	HPLC/DAD	868.50	0.12	-0.69	NO
14	HPLC/UV	887.50	0.11	0.27	NO
15	HPLC/DAD	865.30	-2.22	-0.85	NO
16	HPLC/PDA	881.85	-0.06	-0.02	NO
17	HPLC/DAD	829.90	-5.98	-2.63	NO
18	HPLC/PDA	887.60	2.48	0.27	NO
19	HPLC/MS/MS	831.50	3.73	-2.55	NO
20	HPLC/UV	873.55	0.06	-0.43	NO
Grand Average[3]			879.06		
Total SD			22.06		
Total Median[4]			882.15		
MAD			13.40		
MAD_E			19.87		

[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] Grand average, standard deviation and median.
[4] Median Absolute Deviation Robust estimation of standard deviation; see Appendix for calculations.

Table 18. FLUROXYPYR: representative method of the determination (ITPT2024)

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume µL	Column T°	Detector	Stationary phase (SP) Mobile phase (MP)
2	In-house method	No	acetone	Weight a sample portion diluted in 50 mL acetone, sonicate for 15 min. Dilute 1 mL to 3 mL acetone	1	Initial:70°C, Hold: 1 min, Rate: 30°C/min, Final: 280°C, Hold: 5 min	FID	**SP**: Zebron ZB 17-01 30 m x 0,32 mm; 0,25 µm; Injector temperature: 250°C; Injection ratio: Split, 1:20 **MP**: Helium
4	Manufacturer's method	No	acetonitrile	Weigh a quantity of sample containing 150 mg of sample, dilute with 90 mL ACN swirl and place in ultrasonic bath for 4 min. Cool to ambient temperature and fill to mark with acetonitrile. Filter on anotop 0.45 µm	10	25	PDA 254 nm	**SP**: Zorbax SB C18 250 x 4.6 mm; 5 µm; 1.0 mL/min **MP**: water acid phosphoric acid/acetonitrile (20:80, v/v)
5	In house method	No	acetonitrile	Dilute a sample portion with acetonitrile, sonicate for 15 min.	2	30	DAD 230 nm	**SP**: XTerra RP18 150 x 2.1 mm; 3.5 µm; 0.3 mL/min **MP**: water acid phosphoric acid 0.1%/acetonitrile
7	In-house method	Dicyclo-hexylph-talate	acetone	Sonicate for 2 min, filter on 0.45 µm PTFE syringe.	1	Initial: 65 °C, Hold: 0.5 min, Rate: 50 °C/min, Final: 280 °C, Hold: 6 min	FID	**SP**: TG-5 MS 30 x 0.25 mm; 0.25 µm; Injector temperature: 250°C; Injection ratio: Split, 5:1 **MP**: hydrogen
8	In-house method	No	acetonitrile	Dilute a sample portion with 100 mL acetonitrile	5	40	DAD 220nm	**SP**: Waters Spherisorb ODS2 250 x 46.mm; 5 µm; 1.5 mL/min **MP**: acetonitrile/water acid 0.1% acetic acid (60/40, v/v)
9	In-house method	No	methanol/water (90:10, v/v)	Dissolve sample in 5 mL of water. Fill to mark with methanol. Dilute with methanol. Filter on Anotop 0.45 µm	20	25	MS/MS	**SP**: Phenomenex Gemini C18 150 x 2mm; 3 µm; 0.2 mL/min **MP**: water acid formic acid 0.3%/methanol acid formic acid 0.3%
10	In-house method	No	saponification with KOH solution + methanol	Sonication for 5 mins, wait 24 hours, filter through 0,45µm PTFE disk	5	30	UV-VIS 240 nm	**SP**: Phenomenex Gemini 150 x 4.6mm; 5 µm; 1 mL/min **MP**: acetonitrile/water/acetic acid (49.5:49.5:1)

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume µL	Column T°	Detector	Stationary phase (SP) Mobile phase (MP)
11	Manufacturer's method	No	acetonitrile	Dilute the weighted sample to 50 mL (52.5 mg) and 100 mL (104 mg) with acetonitrile. Sonicate for 5 min and inject	20	25	DAD 254 nm	**SP**: Pinnacle II C18. 150 X 4.6 mm; 5 µm; 1.5 mL/min **MP**: Acetonitrile/Water acid phosphoric acid pH=3 (60:40, v/v)
12	In-house method	No	ethyl acetate	Dilute a weighed sample in ethyl acetate. Sonicate and allow to cool. Make up to volume (25 mL) and further dilute 1:5. Filter on 0.45 µm PTFE.	1	Initial: 65°C; Hold: 0.5 min; Rate: 50°C/min; Final: 280C; Hold: 6mins	FID	**SP**: HP-5MS 30 X 0.25mm; 0.25 µm. Injector temperature: 250°C; Injection ratio: Split, 5:1 **MP**: Helium
14	In-house method	No	acetonitrile	Add 20 mL acetonitrile to sample weighted, sonicate for 10 sec. Add to the mark 50 mL acetonitrile.	1	40	DAD 230 nm	**SP**: Phenomenex Kinetex C18 100 X 4.6mm; 2.6 µm; 1.5 mL/min **MP**: Acetonitrile/Water acid phosphoric acid pH =2 (70:30, v/v)
15	Manufacturer's method	No	acetonitrile/water (50/50, v/v)	Dilute a sample portion in 10 mL of acetonitrile/water (50/50, v/v).	2	50	DAD 235 nm	**SP**: Zorbax Eclipse plus C18 100 X 2.1 mm; 1.8 µm; 0.2 mL/min **MP**: Water acid phosphoric acid 0.1%/Acetonitrile (20:80, v/v)
16	In-house method	Dibutylphthalate	methylisobutylketone	Dilute a sample portion in 25 mL of internal Standard (IS) solution. Sonicate the solution. Filter on 0.45 µm PTFE	1	Initial: 210°C; Hold: 2 min; Rate: 10°C/min; Final: 290°C Hold: 5 min	FID	**SP**: DBWAX 60 mx0.25 mm; 0.25 um
17	In-house method	No	h_2o/tetrahydro-furan (50/50, v/v)	Dilute a sample portion in extraction solvent. Sonicate for 15 min. Filter through 0.2 µm PP disk	10	35	240 nm	**SP**: Accucore XL 250 X 3 mm; 4 µm; 0.9 mL/min **MP**: water acid phosphoric acid 0.5%/acetonitrile (25/75, v/v)
18	Manufacturer's method	diethyl phtalate	ethyl acetate	Weight a sample portion, dilute with 20 mL IS solution in ethyl acetate. Sonicate the solution for 30 min. Filter on 0.2 µm nylon disk.	1	Initial 80°C, Hold 1min, Rate 30°C/min, Final 300°C	FID	**SP**: DB1701 30 m x 0,25mm; 0,25µm Injector temperature: 300°C; Injection ratio: Split, 30:1 **MP**: Helium
19	In-house method	Nicarbazin	acetonitrile 0.1% formic acid	Dilute a sample portion in acetonitrile 0.1% formic acid and sonicate for 15 min	10	32	MS/MS	**SP**: Acquity UPLC HSS T3 Water 100 X 2.1mm; 1.8 µm; 0.350 mL/min **MP**: Water acid acetic acid 0.01% /Acetonitrile acid acetic acid 0.01%

Table 19. BOSCALID: representative method of the determination (ITPT2024)

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume µL	Column T°	Detector	Stationary phase (SP) Mobile phase (MP)
1	In house method	N/A	acetonitrile	Dilute a sample portion in acetonitrile. Sonicate and filter on 0.2 µm	2	NA	PDA 260 nm	**SP**: Aquity 100 x 2.1 mm; 1.7 µm; 1.5 mL/min **MP**: water acid formic acid 0.1%/ acetonitrile
2	In house method	N/A	acetonitrile/water (70:30, v/v)	Dilute a sample portion in 50 mL acetonitrile/water (70:30), sonicate for 15 min and dilute 1:4	3	30	DAD 237 nm	**SP**: Lichropher 100 RP 18 250 x 4 mm; 5 µm; 1.5 mL/min **MP**: water acid phosphoric acid 0.1%/acetonitrile (30:70, v/v)
3	In house method	N/A	10% water/ methanol	Dilute a sample portion with 10% Water/Methanol. Sonicate for 10 min. Filter through 0.45 µm PTFE filter	10	30	UV 220 nm	**SP**: Kinetex C18100A 150 x 4.6 mm; 5 µm; 1 mL/min **MP**: WATER ACID PHOSPHORIC ACID 0.1%/ ACETONITRILE
4	CIPAC MT 673	N/A	acetonitrile/ water	Dilute a sample portion with 50 mL acetonitrile, swirl, and sonicate for 5 min. Add water just below the mark. Wait to cool at ambient temperature and fill to mark with water and mix. Dilute 20 mL of this solution in 50 mL with acetonitrile	10	25	PDA 260 nm	**SP**: Allure C18 250 mm × 4.6 mm; 5 µm; 1.0 mL/min **MP**: a) water + acetonitrile + ammonium acetate (350 mL + 650 mL +770 mg) b) water + acetonitrile + ammonium acetate (100 mL + 900 mL+770 mg)
5	In house method	NA	acetonitrile	Sonicate for 15 min	2	30	UV 270 nm	**SP**: Xterra RP18 150 x 2.1 mm; 3.5 µm; 0.3 mL/min **MP**: water acid phosphoric acid 0.1% /acetonitrile
6	In house method	NA	acetone	Sonicate for 15 minutes. Filter through 0.45 µm nylon filter	10	35	DAD 218 nm	**SP**: Zorbax Eclipse C8 150 x 4.6 mm; 5 µm; 1 mL/min **MP**: water acid 0.1% phosphoric acid /acetonitrile
7	In house method	Dicyclohexylphtalate	acetone	Sonicate for 2 min, filter through 0.45 µm PTFE syringe filter	1	Initial: 65 °C, Hold: 0.5 min, Rate: 50°C/min, Final: 280 °C, Hold: 6 min	FID	**SP**: TG-5 MS 30 m x 0.25 mm; 0.255 µm; Injector temperature: 250°C Injection ratio: Split; 5:1 **MP**: helium

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume µL	Column T°	Detector	Stationary phase (SP) Mobile phase (MP)
8	CIPAC MT 673	NA	water/ acetonitrile	1st step: 10 mL water (to form a slurry) + 50 mL acetonitrile, then sonicate 5 min and dilute up to 100 mL with water (solution 1) / 2nd step: 10 mL of solution 1 diluted to 50 mL with acetonitrile	5	25	DAD 260 nm	**SP**: Luna C18 250 x 4.6 mm; 5 µm; 1.1 mL/min **MP**: a) 350 mL water + 650 ml acetonitrile +770 mg ammonium acetate b)100 ml water + 900 ml acetonitrile +770 mg ammonium acetate
9	In house method	N/A	methanol/ water 90:10	Dissolve sample in 5 mL of water. Fill to mark with methanol. Dilute with methanol and filter 0.45 µm.	20	25	Orbitrap	**SP**: Gemini C18 150 X 2mm; 3 µm; 0.2 mL/min **MP**: a) water - 0.3% formic acid b) methanol - 0.3% formic acid
10	CIPAC MT 673	N/A	acetonitrile/ water (80:20)	Sonicate 5 min. Filter through 0,45 µm PTFE disk	5	25	DAD 260 nm	**SP**: Zorbax Eclipse Plus C18 250 x 4.6 mm; 5 µm; 1.0 mL/min **MP**: acetonitrile: water with ammonium acetate (65:35, v/v)
11	Manufacturer's method	N/A	methanol	Dilute a weighted sample with acetonitrile (50 mL) and analyze.	5	25	DAD 260 nm	**SP**: Pinnacle II C18 150 x 4.6 mm; 5 µm; 1.0 mL/min **MP**: a) water with 770 mg/L ammonium acetate b) acetonitrile
12	In house method	N/A	acetonitrile	Dilute sample weighed in Acetonitrile. Sonicate and allow to cool. Fill up to volume 50 mL and further dilute 1:10. Filter (0.45 µm)	5	25	PDA 260 nm	**SP**: Kinetex C18 100A; 100 x 4.6 mm; 2.6 µm; 1.0 mL/min **MP**: water formic acid 0.1%/acetonitrile (35:65, v/v)
13	In-house method	Proprio-phenone	acetone	Weight a sample portion. Sonicate for 30 min. Dilute with acetonitrile	10	40	DAD 220 nm	**SP**: Zorbax C18 150 x 4.6 mm; 5 µm; 1 mL/min **MP**: water acid phosphoric acid 0.1%/ Acetonitrile (50:50, v/v)
14	In house method	N/A	water 0.1% ammonia/ methanol	Dilute sample weighted with 20 mL water, sonicate for 10 sec. Fill up to the mark with 100 mL methanol, and allow cooling and filtering on 0.2 µm disk	1	40	DAD 280 nm	**SP**: Kinetex C18 100 x 4.6 mm; 5 µm; 1.0 mL/min **MP**: water/methanol (20:80, v/v)
15	Manufacturer's method	N/A	acetonitrile/water (50/50, v/v)	Dilute sample weighted to 25 mL	5	50	DAD 270 nm	**SP**: Zorbax Eclipse Plus C18 100 x 2.1 mm; 1.8 µm; 0.2 mL/min **MP**: water/acetonitrile (50:50, v/v)

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume µL	Column T°	Detector	Stationary phase (SP) Mobile phase (MP)
16	CIPAC MT 673	NA	acetonitrile/water (90/10, v/v)	Disperse the sample with 10 mL of water into a 100 mL volumetric flask, add 50 mL of acetonitrile, sonicate for 5 minutes and fill up to volume at 20°C with acetonitrile. Transfer exactly 10 mL of this solution into a 50 mL volumetric flask and fill up to volume with acetonitrile. Filter through a 0.45 µm PTFE filter	5	25	PDA 260 nm	**SP**: Zorbax Eclipse XDB C18 150 x 4.6 mm id; 3.5 µm; 1 mL/min **MP**: (water – acetonitrile – ammonium acetate 350 mL + 650 mL + 770 mg) – (water – acetonitrile – ammonium acetate 100 mL + 900 mL + 770 mg) (40-60 v/v)
17	In house method	NA	water/tetrahydro-furan 50/50 (v/v)	Dilute sample portion in extraction solvent, sonicate for 10 min. Filter through 0.2 µm PP disk	10	35	DAD 252 nm	**SP**: Nucleodur C18 250 x 3mm; 5 µm; 0.3 mL/min **MP**: water/acetonitrile (25:75, v/v)
18	In house method	NA	acetonitrile/water (50/50, v/v)	Dilute sample portion in 10mL water, shake for 10 min, and add 50 mL acetonitrile. Sonicate 30 min and fill up to 100 mL with water. Dilute 1 mL of solution to 5 mL with acetonitrile. Filter through nylon disk 0,2 µm	0,5	40	PDA 260 nm	**SP**: Biphenyl, 100 x 2.1 mm; 2.6 µm; 0.3 mL/min **MP**: water (0.1% formic acid)/acetonitrile (35:65 v/v)
19	In house method	Triphenylp hosphate	acetonitrile 0.1% acid formic	Sonicate for 15 min	10	40	MS/MS	**SP**: Accucore 100 x 2.1 mm; 2.6 µm; 0.4 mL/min **MP**: a) water containing 5 mm ammonium formate and 0.01% formic acid b) Methanol containing 5 mm ammonium formate and 0.01% formic acid
20	In house method	N/A	acetone	Dissolve a sample portion in acetone, then shake for 1 min, dilute 1 mL to 20 mL and inject in LC.	5	40	UV/Vis 230 nm	**SP**: Ascentis Express RP-Amide 75 x 2.1 mm; 2.7 µm; 0.4 mL/min **MP**: a) KH2PO4 138 mg/L + phosphoric acid conc 100 µL/L b) methanol

Table 20. BENTAZONE: representative method of the determination (ITPT2024)

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume µL	Column T°	Detector	Stationary phase (SP) Mobile phase (MP)
1	In house method	N/A	acetonitrile	Dilute sample portion in acetonitrile and sonicate. Filter on 0.2 µm PTFE.	2	NA	PDA 340 nm	**SP**: Acquity UHPLC BEH 100 × 2.1 mm; 1.7 µm; 0.4 mL/min **MP**: Water acid formic 0.1%/Acetonitrile
3	In house method	NA	10% water in acetonitrile	Dilute a sample portion in extraction solvent. Sonicate for 10 min. Filter through 0.45 µm PTFE and analyze	10	30	DAD 220 nm	**SP**: Kinetex C18 150 x 4.6 mm; 5 µm; 1 mL/min **MP**: Water acid formic 0.1%/Acetonitrile
4	CIPAC MT 366	NA	methanol/sodium acetate buffer (40+60, v/v)	Dilute a sample portion with 4 mL FMethanol. Add 6 mL of buffer solution and fill to mark with mobile phase. Swirl and filter on 0.45 µm filter.	10	25	PDA 340 nm	**SP**: Lichrospher 100RP 250 x 4,6 mm; 5 µm; 1.0 mL/min **MP**: Methanol/Sodium acetate buffer 0.075 N (40:60, v/v)
6	In house method	N/A	acetone	Dilute a sample portion with acetone. Sonicate for 15 min. Filter through 0,45 µm nylon filter	10	35	DAD 218 nm	**SP**: Zorbax Eclipse C8 150 x 4.6 mm; 5 µm; 1 mL/min **MP**: Acetonitrile/water phosphoric acid 0.1%
7	In house method	NA	acetonitrile	Dilute a sample portion with acetonitrile. Sonicate for 8 min. Filter through 0.22 µm PTFE filter	0.5	25	PDA 240nm	**SP**: Kinetex C18 100 x 2.1 mm; 2.6 µm; 0.4 mL/min **MP**: Acetonitrile/water phosphoric acid 0.1%
8	CIPAC MT 366	NA	methanol + sodium acetate buffer	Dilute a sample portion with 2 mL Methanol + 3 mL sodium acetate buffer. Dilute up to 50 mL with mobile phase (methanol: sodium acetate buffer 40:60 v/v)	20	30	DAD 340 nm	**SP**: Phenomenex Luna C18, 250 x 4.6mm; 5 µm; 0.8 mL/min **MP**: Methanol/sodium acetate buffer (40: 60 v/v
9	In house method	N/A	methanol/water 90:10	Dissolve sample in 5mL of water. Fill to mark with methanol. Dilute with methanol and filtered on 0.45 µm filter	20	25	UV Vis 302 nm	**SP**: Gemini C18, 150 x 2 mm; 3 µm; 0.2 mL/min **MP**: a) water 0.3% formic acid b) methanol 0.3% formic acid
10	CIPAC MT 366	N/A	methanol /acetate buffer solution ph 6 (40:60)	Dilute a sample portion with 4 mL Methanol. Add 6 mL of buffer solution and fill to mark with mobile phase. Swirl and filter on 0.45 µm filter	10	40	UV Vis 340 nm	**SP**: Zorbax Eclipse Plus C18, 250 mm x 4,6 mm; 5 µm; 1 mL/min **MP**: methanol/acetate buffer pH6 (40:60, v/v)

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume µL	Column T°	Detector	Stationary phase (SP) Mobile phase (MP)
11	CIPAC MT 366	N/A	acetonitrile	Dilute a sample portion with acetonitrile (50 mL) and analysed.	20	25	DAD 340 nm	**SP**: Pinnacle II C18 150 x 4.6 mm; 5 µm; 1.0 mL/min **MP**: methanol/ Na-Acetate 0.075 N buffer pH 6 with acetic acid (40:60, v/v)
12	In house method	N/A	acetonitrile	Dilute a sample portion with acetonitrile. Sonicate and allowed to cool. Fill up to volume (50 mL) and further dilute 1:10. Filter on 0.45 µm filter.	5	25	PAD 250 nm	**SP**: Kinetix C18 100A 100 x 4,6 mm; 2.6 µm; 1.0 mL/min **MP**: acetonitrile/water acid formic 0.1% (65:35, v/v)
13	In house method	Propiophenone	acetonitrile	Dilute a sample portion in acetonitrile. Sonicate for 30 min.	1	40	DAD 220 nm	**SP**: Zorbax SB C18 150 x 4.6 mm; 5 µm; 1 mL/min **MP**: acetonitrile/water acid phosphoric acid 0.1% (50:50, v/v)
14	In house method	NA	water 0.1 % ammonia	Sample portion added with 20 mL water (0.1% ammonia). Sonicate for 10 min. Fill up to the mark (100 mL) water (0.1% ammonia)	5	40	UV Vis 304 nm	**SP**: Phenomenex Gemini NX C18, 50 x 4.6 mm; 3 µm; 1.5 mL/min **MP**: methanol/water acid phosphoric acid pH 2 (50:50, v/v)
15	Manufacturer's method	NA	acetonitrile	Dilute a sample portion with 50 mL acetonitrile	2	40	DAD 230 nm	**SP**: Zorbax Eclipse Plus C18, 150 x 4.6 mm; 5 µm; 0.8 mL/min **MP**: acetonitrile/water acid phosphoric acid 0.5% (70:30, v/v)
16	In house method	N/A	acetonitrile/water /phosphoric acid (40/60/0.1 v/v/v)	Dissolve a sample portion in 200 mL of acetonitrile-water phosphoric acid (40/60/0.1 v/v/v). Sonicate for 10 min and filter through a 0.45 µm PTFE filter	10	40	PDA 300 nm	**SP**: Kromasil C18, 100°A 250 mm × 4.6 mm; 5 µm; 1.0 mL/min **MP**: 40% acetonitrile + 0.1% phosphoric acid/ 60% water + 0.1% phosphoric acid (40/60 v/v)
17	In house method	NA	water/tetrahydro-furan 50/50 (v/v)	Dilute a sample portion in extraction solvent. Sonicate for 15 min. Filter through 0.2 µm PP disk	10	35	DAD 302 nm	**SP**: Kromasil C18 250 x 3 mm; 5 µm; 0.3 mL/min **MP**: 35% Water acidified with 0,5 % phosphoric acid/65% Acetonitrile

ID Lab	Reference method	Internal standard	Extractants	Sample preparation	Injection volume µL	Column T°	Detector	Stationary phase (SP) Mobile phase (MP)
18	CIPAC MT 366	NA	methanol	Dilute a sample portion in 50 mL methanol. Sonicate for 30 min. Dilute 1 mL in 20 mL of buffer (acetate de Na 0,075N pH 6 -CH3OH: 50-50). Filter through nylon disk 0,2 µm	1	40	PDA 340 nm	**SP**: Biphenyl 100 mm x 2.1 mm; 2.6 µm; 0.3 mL/min **MP**: methanol/sodium acetate 0.075N pH 6 Acetic acid
19	In house method	Nicarbazin	Water/Acetonitrile/Acetone	Dilute a sample portion in extraction solvent. Sonicate for 15 min	10	32	MS/MS	**SP**: Acquity 100 x 2,1 mm; 1.8 µm; 0.350 mL/min **MP**: a) 0.01 % acetic acid in water b) 0.01 % acetic acid in Acetonitrile
20	In house method	NA	Acetone	Dilute a sample portion in acetone, then shake for 1 min. Dilute 1 mL to 40 mL in acetone and inject in LC	5	40	UV Vis 230 nm	**SP**: Ascentis Express RP-Amide; 75 x 2.1 mm; 2.7 µm; 0.4 mL/min **MP**: a) KH2PO4 136 mg/L + phosphoric acid 100 µL/L b) methanol

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APPENDIX A
The announcement letter

DIPARTIMENTO
AMBIENTE E SALUTE

ANNOUNCEMENT/INVITATION
ITPT2024

Dear Colleagues,

We herewith cordially invite you to participate in the Italian Proficiency Test on the analysis of PPPs in EC, SG and WG. The Italian Laboratory of National Institute of Health – Department of Environment and Health organize this exercise, in the framework of the collaboration with the Health Ministry.
We scheduled to run the ITPT2024 from 15th of January until 30th of April 2024.

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 they take the necessary measures for quality improvement.

TEST ITEM
Ca. 10g of PPP test Item will be shipped to each participating laboratory.
To participant it ask to analyze three products containing three active substances in two different days.

TARGET ANALYTES
The analytes are:

Active Substance	Conc (g/100g)	Formulation
Fluroxypyr	29.2	EC
Boscalid	50	WG
Bentazone	87	SG

SHIPMENT AND RECEIPT OF THE TEST ITEM
We planned the shipment of the Test Item around 15th of January 2024. If any laboratory will be on holiday in the week of the shipment, please inform the organizer to rearrange shipment.
The sample will be shipped at room temperature.
Participants must check the integrity and condition of the materials upon receipt and to report within 48h if they accept the materials or not.

IMPORTANT DATES
- Shipment of the Test Items around 15th of January 2024.
- Submission of results and method information by 30th of April 2024.

Istituto Superiore di Sanità
Dipartimento /
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DIPARTIMENTO
AMBIENTE E SALUTE

PARTICIPATION FEE
The participation is free of charge.

RELEVANT DOCUMENTS
Copies of SDS will be send via e-mail separately.
Participants are encouraged to employ the method typically run in their lab for these compounds.
Copies of the methods will be send to participants that asked them, separately.

OTHER INFORMATION
Only the information of the laboratory and name of participant will be publish on the report.
The correlation between laboratory (name of participant, name of laboratory) and number of laboratory will be consider confidential and not publish on the report.

CALENDAR for the ITPT2024

Activity	Dates
Opening of the ITPT2024	7 November 2023
Confirm the participation	5 December 2023
Shipment of the ITPT2024 Test Item	15 January 2024
Confirmation of Sample Receipt and Acceptance	Within 48 h of receipt
Result Submission	30 January – 30 April 2024
Preliminary Report	May 2024
Final Report	June 2024

SUPPORT AND CONTACT INFORMATION

For any questions about the ITPT2024, please mail to angela.santilio@iss.it; silvana.girolimetti@iss.it

Best regards,

The ITPT2023 Organizing Team

Angela Santilio

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APPENDIX B
Calendar and list of participants

CALENDAR for the ITPT2024

Activity	Dates
Opening of the ITPT2024	7th November 2023
Confirm the participation	5th December 2023
Shipment of the ITPT-PPP03 Test Item	15th January 2024
Confirmation of Sample Receipt and Acceptance	Within 48 h of receipt
Result Submission	30th January – 30th April 2024
Preliminary Report	June 2024
Final Report	July 2024

LIST OF PARTICIPANTS

Italian participants

Arianna Palchetti, Beatrix Ladurner	*Laboratorio analisi alimenti e sicurezza dei prodotti – APPA BZ*
Luigi Bazzani Diego Tamoni Chiara Cavecchia	*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*
Tiziana Generali	*Istituto Superiore di Sanità, Roma*
Alessandra Giuliani	*ARPA Lazio - Servizio Ambiente e Salute -Dipartimento di Prevenzione e Laboratorio Integrato -Sede territoriale di Roma*
Rossana Scarpone	*Istituto Zooprofilattico dell'Abruzzo e del Molise G. Caporale*
Gianni Formenton	*ARPAV – Verona*

European participants

Christoph Czerwenka	*AGES Group for contaminant and special analysis, Austrian Agency for Health and Food Safety, Austria*
Florentina Ciotea	*National Phytosanitary Authority, Romania*
Sabine Castelle	*Service Commun des laboratories- DGCCRF – DGDDI*
Claudia Vinke Kristina Pape	*Federal Office of Consumer Protection and Food Safety, Laboratory for formulation chemistry, Germany*

Martin Karkov Kristensen	*Laboratory for chemistry and microbiology, Danish Technological Institute, Denmark*
Isabelle Monisse	*AFSCA, Belgium*
Kati Hakala	*Finnish Food Authority, Finland*
Helen Karasali	*Laboratory of chemical Control of Pesticide, Benaki Phytopathological Institute, Greece*
Elaine Devaney	*Pesticide formulation laboratory, Ireland*
Hana Slampová	*UKZUZ Central Institute for Supervising and Testing in Agriculture, National Reference laboratory, Department of testing Plant Protection Products, Czech Republic*
Aleksander Vladimirov	*CLCT Central laboratory for chemical testing and control Bulgarian Food Safety Agency, Bulgary*
Maria Baes	*Walloon Agricultural Research Centre (CRA-W), Belgium*
Javier Garcìa-Hierro Navas	*Laboratorio Arbitral Agroalimentario, Spain*

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. 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. It 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.

Horwits Ratio. The Horwits ratio is a normalized performance parameter indicating the acceptability of methods of analysis with respect to among-laboratory precision (reproducibility).

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 - μ) / σ, 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. It 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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