



CURRENTA 

# 283 Metribuzin

CIPAC meeting 2020

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Currenta GmbH & Co. OHG

On behalf of Bayer AG, Crop Science Division and Jiangsu Seven Continent

# Background and Objective

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## Background:

- On the CIPAC-meeting 2019 held in Braunschweig Jiangsu Seven Continent presented a GC-method for the determination of Metribuzin in TGAI and SC, WG and WP formulation types. The applicability of the method has been demonstrated by a small scale trial within Chinese laboratories.
- During the 2019 CIPAC-meeting Bayer AG, Crop Science Division and Jiangsu Seven Continent agreed to perform a joint collaborative full scale trial on Metribuzin to support the renewal of the respective FAO specification. It was also agreed that the joint trial should be operated by Michael Haustein, Currenta GmbH & Co. OHG.

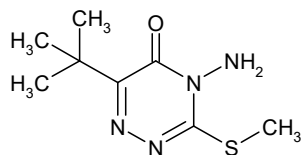
## Objective:

- Present the outcome of the full validation to demonstrate that CIPAC method (CIPAC Doc No. CIPAC/5253/m) is suitable for the determination of Metribuzin in technical grade material and in SC, WP and WG formulation types.

# Metribuzin (Active Substance)

- Common name: METRIBUZIN
- Chemical name: 4-amino-6-tert-butyl-4,5-dihydro-3-methylthio-1,2,4-triazin-5-one
- CAS No.: 21087-64-9
- Trade names: Mistral, Sencor, others

• Structure:



- Molecular Formula: C<sub>8</sub> H<sub>14</sub> N<sub>4</sub> O S
- Molar Mass: 214.3 g/mol
- Melting Point: 125.9 °C
- Solubility: Dichloromethane, 2-Propanol, Polyethyleneglycol, Acetone, Ethylacetate, Acetonitrile, Dimethylsulfoxide > 250 g/L; Xylene 60 g/L, water 1.05 g/L (all at 20°C)
- Description: white fine needles, with weak, not characteristic odour
- Activity: Herbicide

# Outline of the Method

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## Sample Preparation:

The homogenized sample containing Metribuzin is dissolved in Dimethylacetamide (DMAC) and chromatographed by capillary gas chromatography with split injection and detection by flame ionization (FID).

The quantification is performed according to the internal standard method (ISTD) using Dipentylphthalate as internal standard.

## Outline of the Method

Method parameters	
Column	Fused silica, DB-5, 30 m, 0.32 mm I.D., 0.25 µm film
Injector type	split
Split ratio	1:20
Injection volume	0.2 µL
Injection temperature	250 °C
Detector type / -temperature	FID / 300 °C
Oven temperature	220 °C (isothermal)
Carrier gas / flow	Helium / 2.5 mL/min
Running time	10 minutes
Retention times	Metribuzin approx. 2.3 min
	Dipentylphthalate approx. 3.8 min

# Participants

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- 27 respondents to the CIPAC information sheet 321
- The trial was originally limited to maximum of 15 participating laboratories due to the availability of samples and later expanded to 18 laboratories due to the wide interest. The samples were dispatched to the first 18 labs that responded.
- 17 participants sent their results within the requested time
- One laboratory could not reply in time due to restrictions caused by the COVID-19 crisis
- Participants were from Asia, Europe and North- and South America
  - Argentina, China, Czech Republik, Denmark, Germany, Greece, Italy, Ireland, Romania, Switzerland, USA

# Participants

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- 11 of the participating laboratories used Helium as a carrier gas as described in the original method.
- 6 participants used Hydrogen or Nitrogen, respectively, in deviation of the default.
- The results and statistical evaluations were presented of:
  - The 11 laboratories using Helium as carrier gas
  - The full set of 17 participants

## List of Participants (in alphabetical order)

Participant	Company / Institute
Greco, Cornel	ALCHIMEX S.A. 63-Alexandru Constantinescu, sector 1 011472 Bucharest Romania
Schaller, Ulrich	Agroscope Pflanzenschutzchemie Müller-Thurgau-Strasse 29 8820 Wädenswil Switzerland
Schulz, Friedhelm	Bayer AG, Crop Science Division Research & Development, Small Molecules Research, Product Chemistry Analytics Alfred-Nobel-Str. 50, 40789 Monheim am Rhein Germany
Vinke, Claudia	Bundesamt für Verbraucherschutz und Lebensmittelsicherheit Referat Pflanzenschutz Messeweg 11/12, 38104 Braunschweig Germany



## List of Participants (in alphabetical order)

Participant	Company / Institute
Karassali, Helen	Benaki Phytopathological Institute 8 Stefanou Delta street, 14561 Kifissia, Athens Greece
Haustein, Michael	Currenta GmbH & Co. OHG Division Analytics, Production Analytics 41538 Dormagen Germany
Osterballe Pedersen, Christina	Danish Technological Institute Teknologisk Institut Kemisk og Mikrobiologisk Laboratorium Kongsvang Allé 29 8000 Aarhus C Denmark
Santilio, Angela	Istituto Superiore di Sanità (National Institute of Health) Department of Environment and Health (Dipartimento Ambiente e Salute) ECASS Section (Reparto ECASS) Viale Regina Elena, 299 00161 Rome Italy

## List of Participants (in alphabetical order)

Participant	Company / Institute
Lee, Jacky	Jiangsu Seven Continent 7F, Guotai Times Plaza A, Renmin Road, Zhangjiagang, Jiangsu Province, China
Belart, Selma	Laboratorio de Plaguicidas y Formulados SENASA Av. Huergo 1001 - 1107 CABA Argentina
McManus, Kenneth	Maryland Department of Agriculture 50 Harry S Truman Parkway Annapolis, MD 21401 USA
Ciotea, Florentina	National Phytosanitary Authority Voluntari Bvd. No. 11, Voluntari Town, Ilfov County, Romania
Li, Hongxia	NutricheM Laboratory Co., Ltd. No. 27, Life Science Park Road, Changping Dist., Beijing 102206 China

## List of Participants (in alphabetical order)

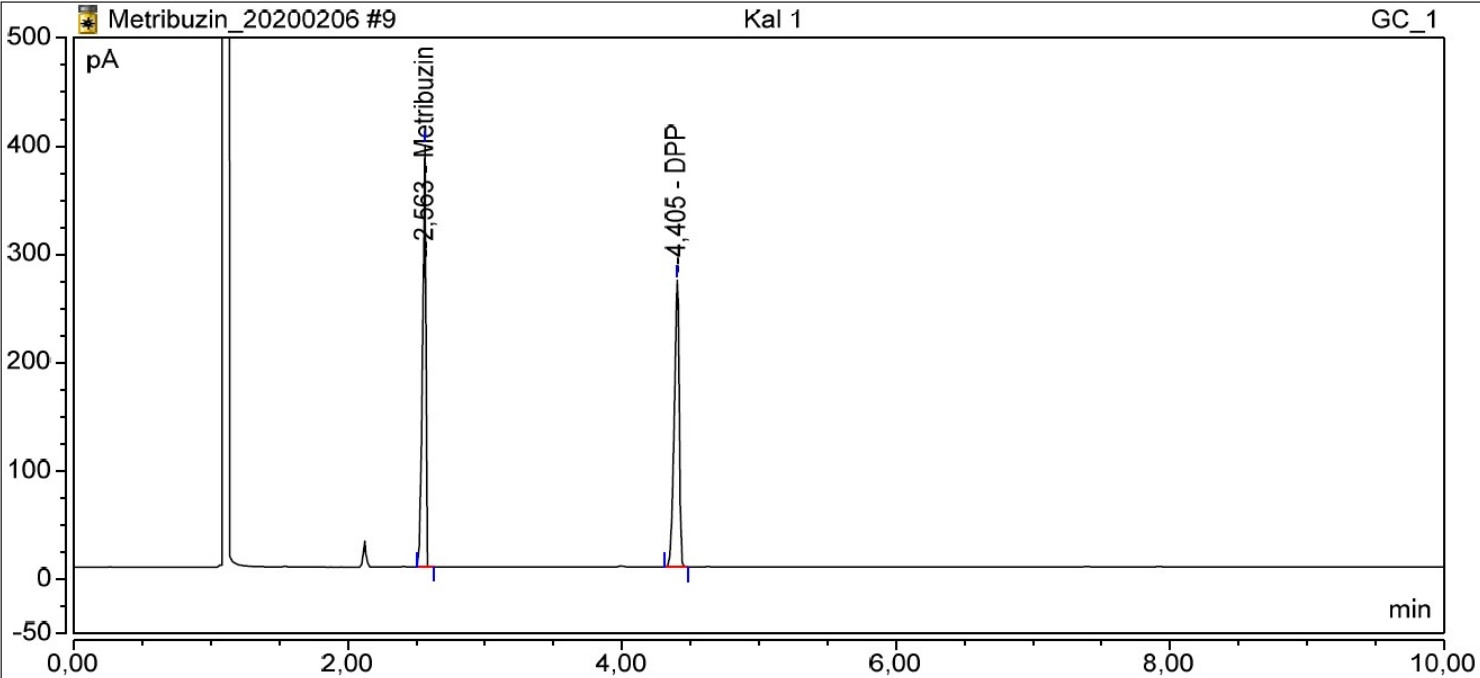
Participant	Company / Institute
Joseph, Rachel	ROTAM RESEARCH LABORATORY No. 233, Songjiagang Road, Zhoushi Town, Kunshan, Jiangsu China
Garvey, Jim	Pesticide Control Laboratory, Department of Agriculture, Food and the Marine Backweston Laboratory Complex, Backweston, Celbridge, Co. Kildare, Ireland
Mink, Christian	Syngenta Crop Protection AG Breitenloh 5, 4333 Münchwilen Switzerland
Novakova, Olga	UKZUZ (CENTRAL INSTITUTE FOR SUPERVISING AND TESTING IN AGRICULTURE) National Reference Laboratory Department of Testing Plant Protection Products Zemědělská 1a, 613 00 Brno Czech Republic

# Samples

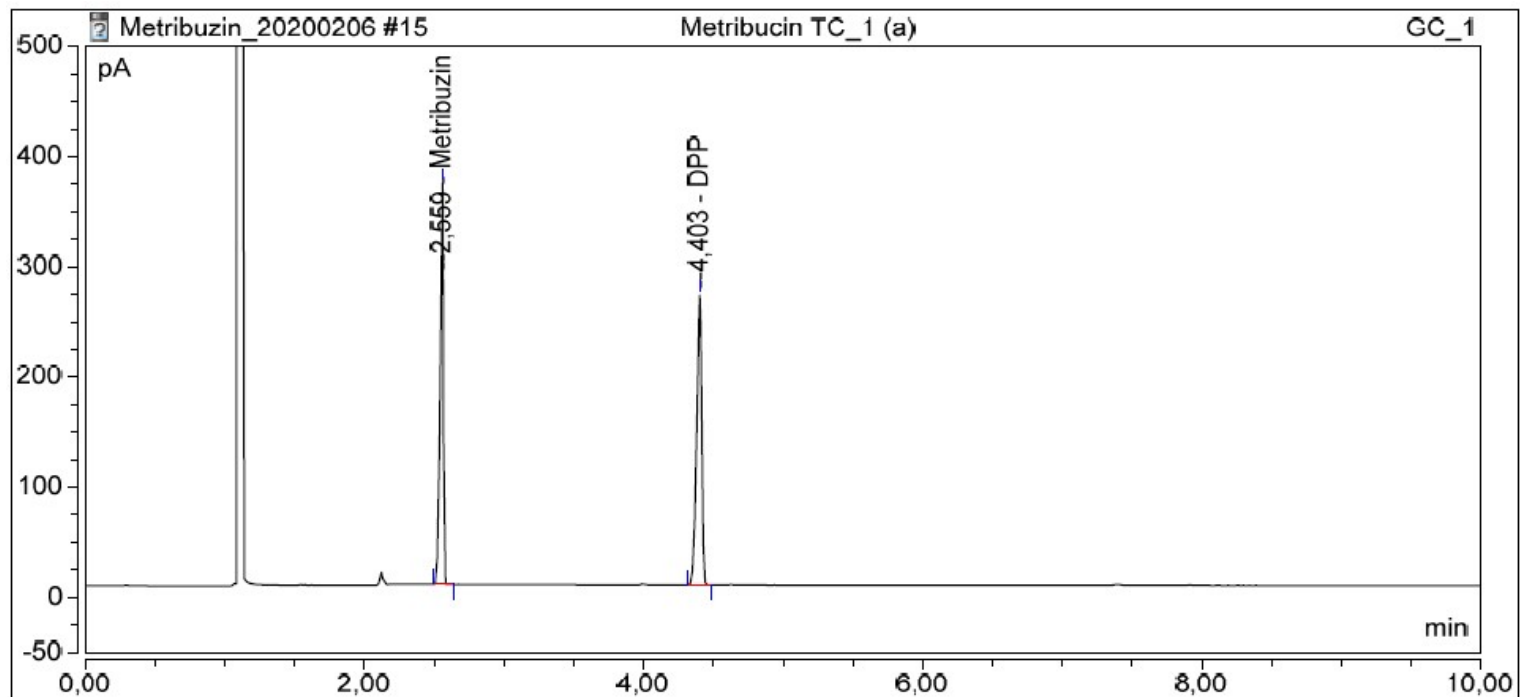
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- Metribuzin technical sample 1 (Metribuzin TC\_1)
- Metribuzin technical sample 2 (Metribuzin TC\_2)
- Metribuzin WG 70 – 1 (Metribuzin WG 70)
- Metribuzin WG 70 – 2 (Metribuzin 70 % WG)
- Metribuzin WP 70 – 1 (Metribuzin WP 70)
- Metribuzin WP 70 – 2 (Metribuzin 70 % WP)
- Metribuzin SC 600, 522 g/kg Metribuzin (Metribuzin SC 600)
- Metribuzin SC 480 - 1, 414 g/kg Metribuzin (Metribuzin SC 480)
- Metribuzin SC 480 – 2 (Metribuzin 42 % SC)

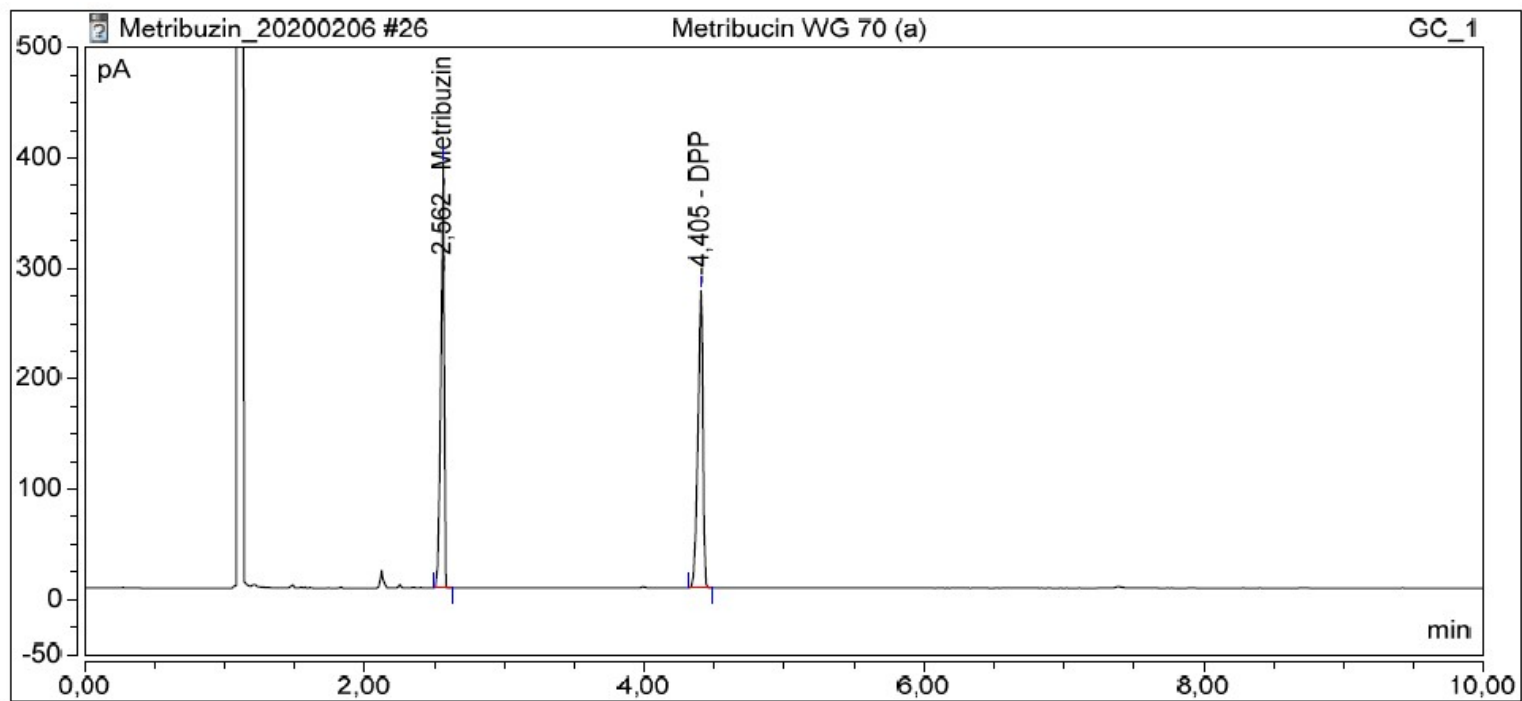
# Typical chromatogram - Calibration



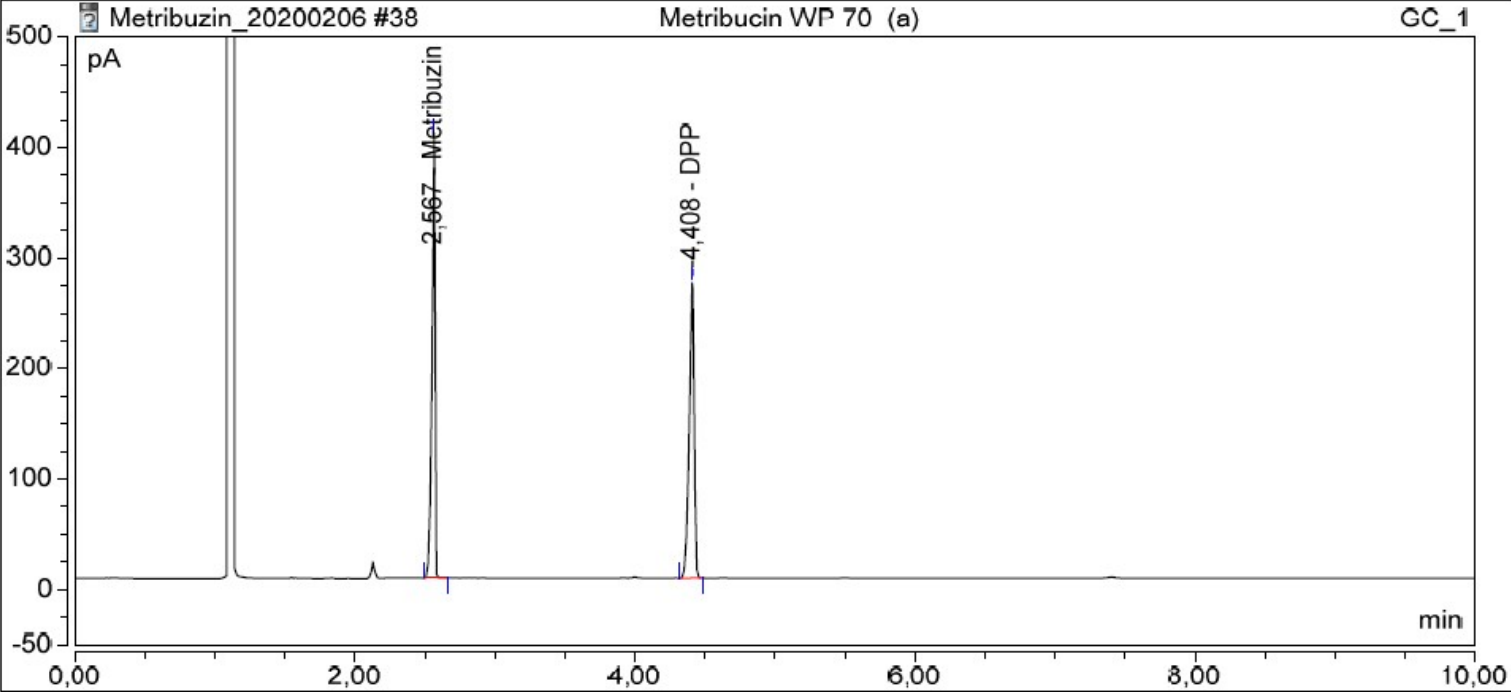
# Typical chromatogram – technical sample



# Typical chromatogram – WG 70

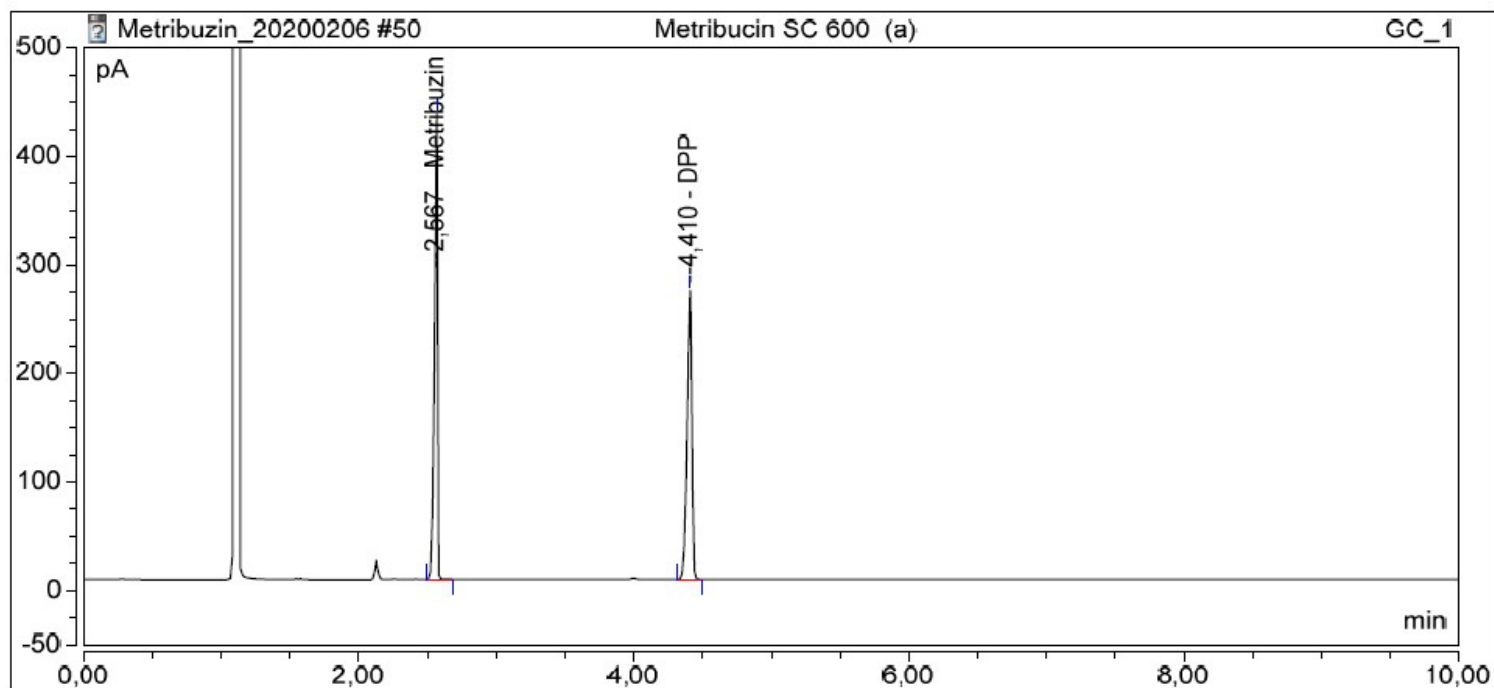


# Typical chromatogram – WP 70

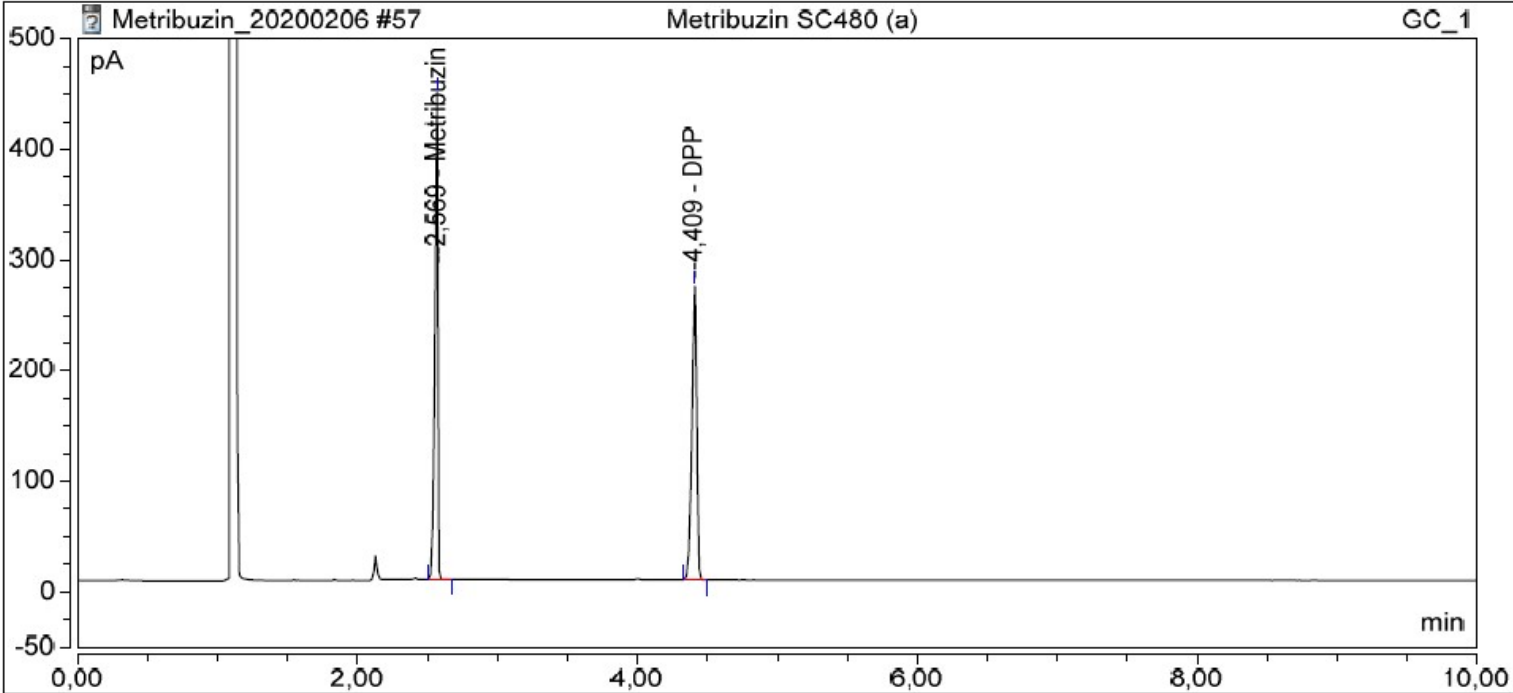




# Typical chromatogram – SC 600



# Typical chromatogram – SC 480

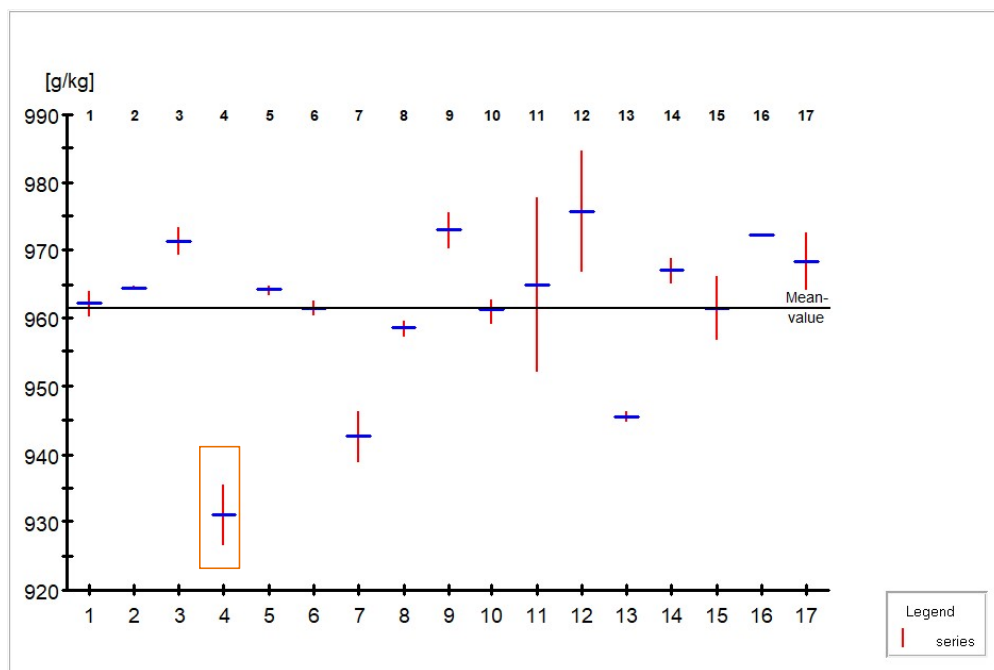


## Statistical evaluation

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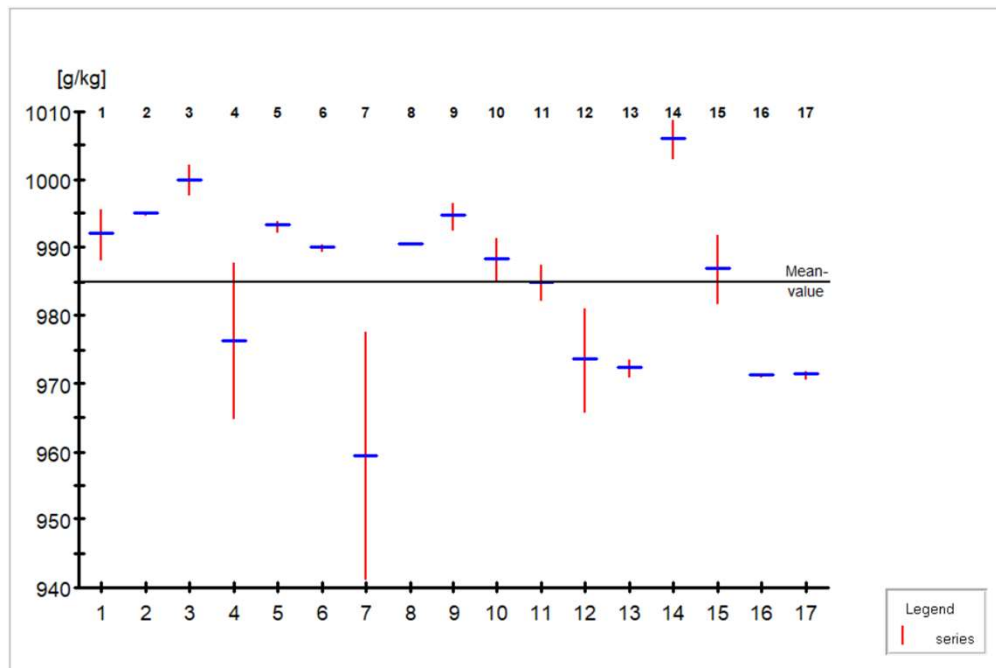
- In summary it can be stated that the method deviations, noted by the participants, were deemed not to affect the analytical results significantly and therefore all data sets were included within the statistical assessment. However, it is obvious that change of the carrier gas from Helium to Hydrogen or Nitrogen, respectively, lowers the total reproducibility leading to a short failure of the HorRat criterion in 2 of 9 samples.
- Therefore, two statistical evaluations, once with the full set of participating laboratories (17) and twice with the 11 participants using Helium as a carrier gas are presented
- Statistical evaluation was carried out according to ISO 5725 using Grubbs outlier/straggler test on a 1%/5% significance level, respectively.

# Metribuzin TC\_1 (full set of 17 participants)



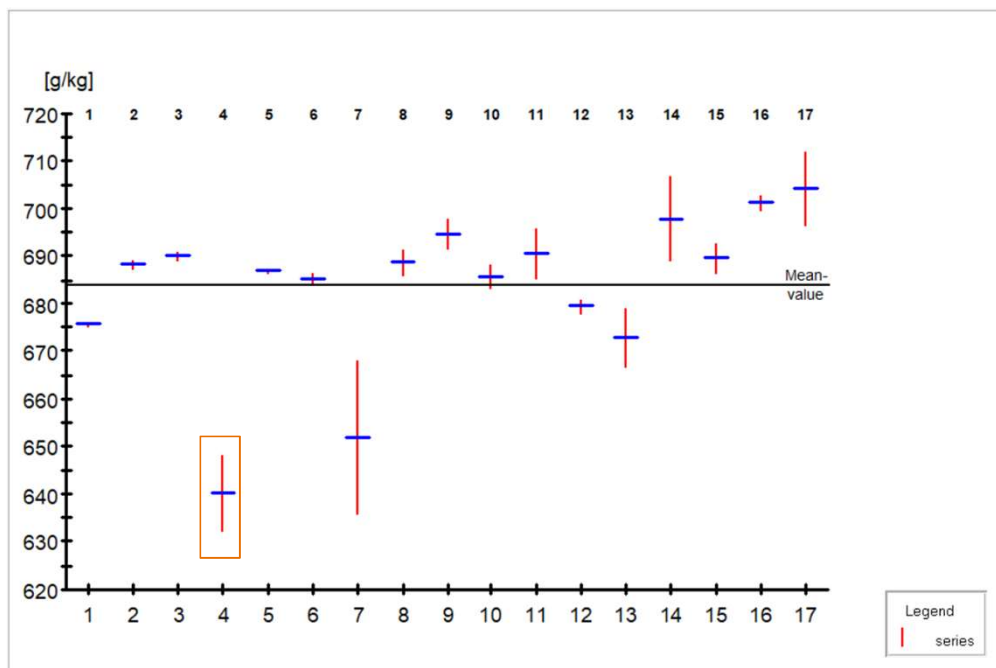
Mean value:	961.57 g/kg
$S_r$ :	6.15
$S_R$ :	12.51
$RSD_R$ :	1.30
$RSD_{R(Hor)}$ :	2.01
HorRat:	0.65
Outlier (Grubbs):	none
Straggler (Grubbs)	lower (lab 4)

# Metribuzin TC\_2 (full set of 17 participants)



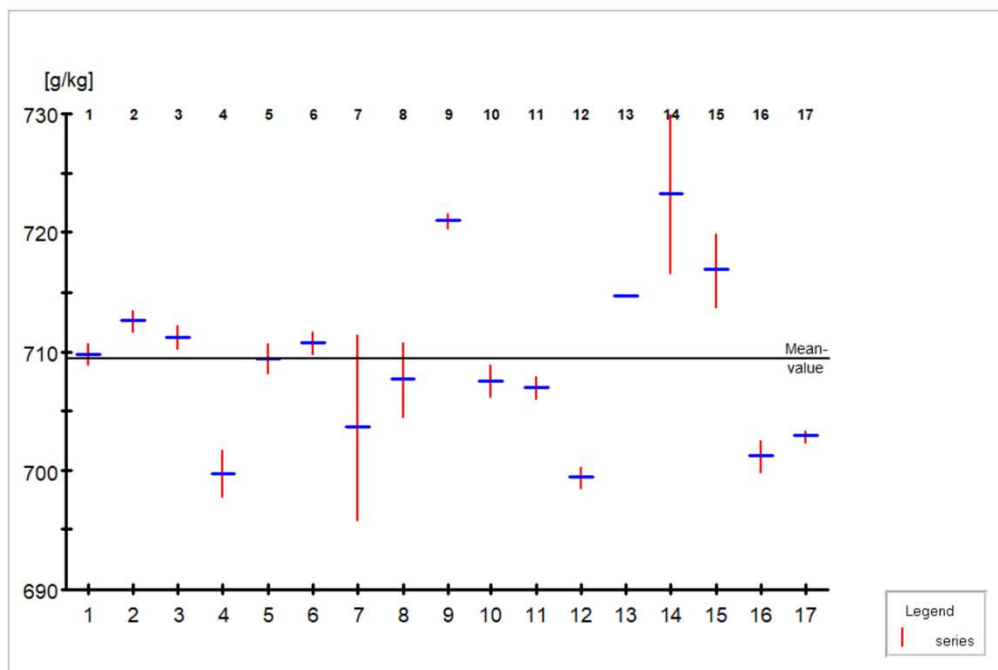
Mean value:	985.07 g/kg
S <sub>r</sub> :	8.24
S <sub>R</sub> :	13.66
RSD <sub>R</sub> :	1.39
RSD <sub>R (Hor)</sub> :	2.00
HorRat:	0.70
Outlier (Grubbs):	none
Straggler (Grubbs):	none

# Metribuzin WG 70 (full set of 17 participants)



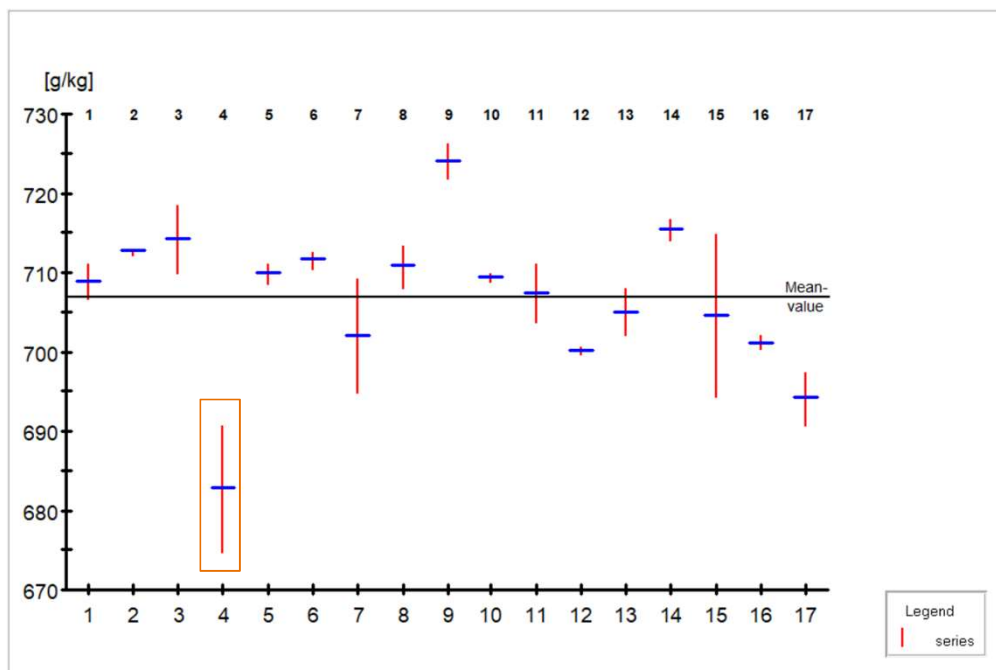
Mean value:	683.84 g/kg
$S_r$ :	7.97
$S_R$ :	17.39
$RSD_R$ :	2.54
$RSD_{R(Hor)}$ :	2.12
HorRat:	1.20
Outlier (Grubbs):	none
Straggler (Grubbs)	lower (lab 4)

# Metribuzin 70 % WG (full set of 17 participants)



Mean value:	709.35 g/kg
$s_p$ :	3.99
$s_R$ :	7.52
$RSD_R$ :	1.06
$RSD_{R(Hor)}$ :	2.11
HorRat:	0.50
Outlier (Grubbs):	none
Straggler (Grubbs)	none

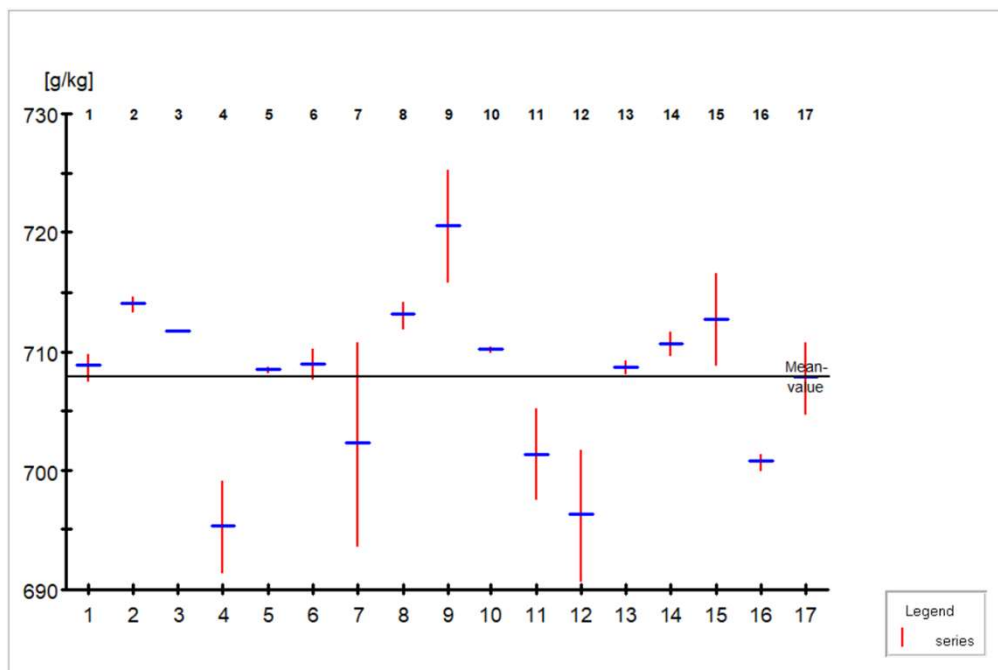
# Metribuzin WP 70 (full set of 17 participants)



Mean value:	706.74 g/kg
$s_r$ :	5.80
$s_R$ :	10.10
$RSD_R$ :	1.43
$RSD_{R(Hor)}$ :	2.11
HorRat:	0.68
Outlier (Grubbs):	none
Straggler (Grubbs)	lower (lab 4)

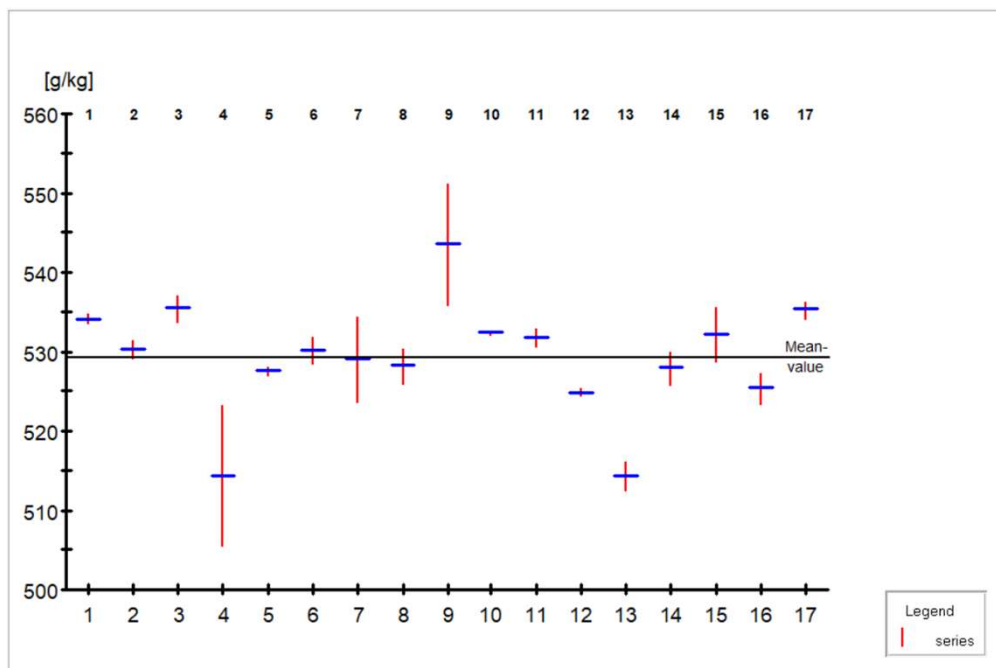


# Metribuzin 70 % WP (full set of 17 participants)



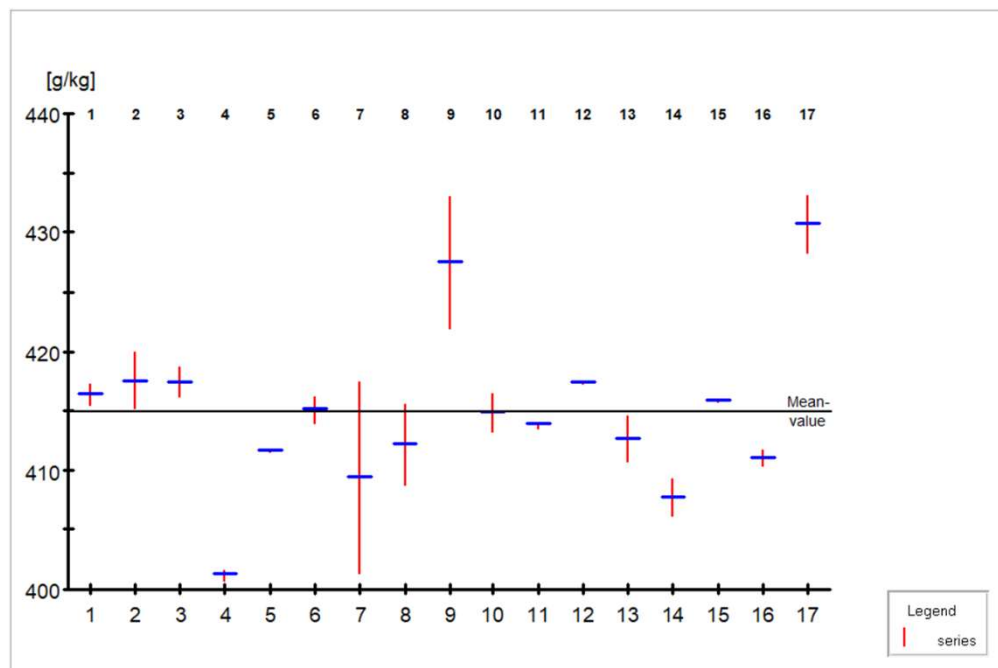
Mean value:	707.77 g/kg
$s_r$ :	4.58
$s_R$ :	7.35
$RSD_R$ :	1.04
$RSD_{R(Hor)}$ :	2.11
HorRat:	0.49
Outlier (Grubbs):	none
Straggler (Grubbs)	none

# Metribuzin SC 600 (full set of 17 participants)



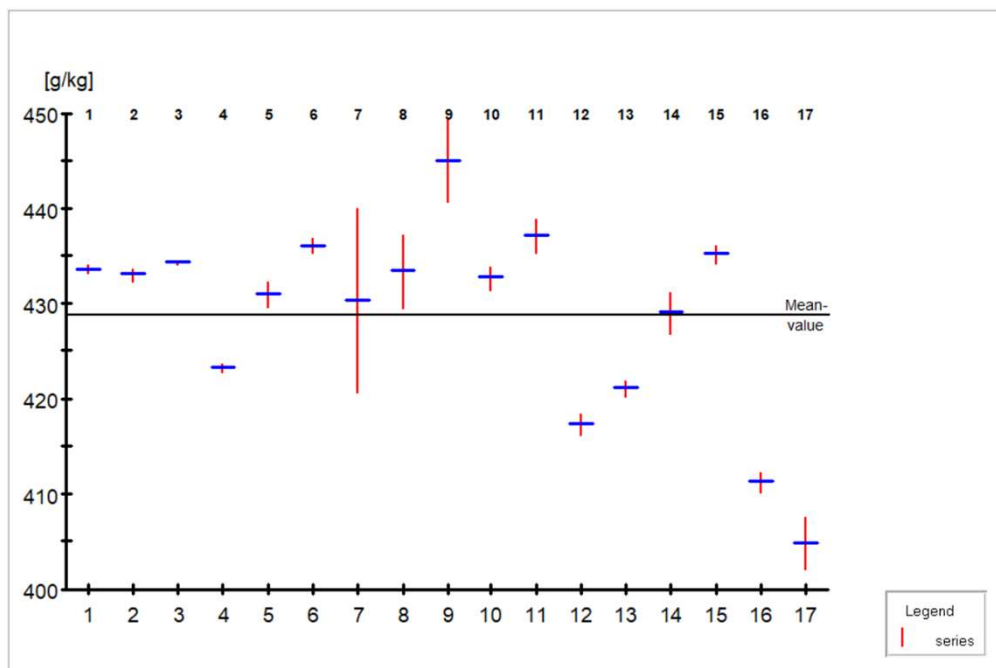
Mean value:	529.25 g/kg
$S_r$ :	4.81
$S_R$ :	7.90
$RSD_R$ :	1.49
$RSD_{R(Hor)}$ :	2.20
HorRat:	0.68
Outlier (Grubbs):	none
Straggler (Grubbs)	none

# Metribuzin SC 480 (full set of 17 participants)



Mean value:	414.87 g/kg
$s_r$ :	3.87
$s_R$ :	7.34
$RSD_R$ :	1.77
$RSD_{R(Hor)}$ :	2.28
HorRat:	0.78
Outlier (Grubbs):	none
Straggler (Grubbs)	none

# Metribuzin 42 % SC (full set of 17 participants)



Mean value:	428.81 g/kg
$S_r$ :	4.15
$S_R$ :	10.55
$RSD_R$ :	2.46
$RSD_{R(Hor)}$ :	2.27
HorRat:	1.08
Outlier (Grubbs):	none
Straggler (Grubbs)	none

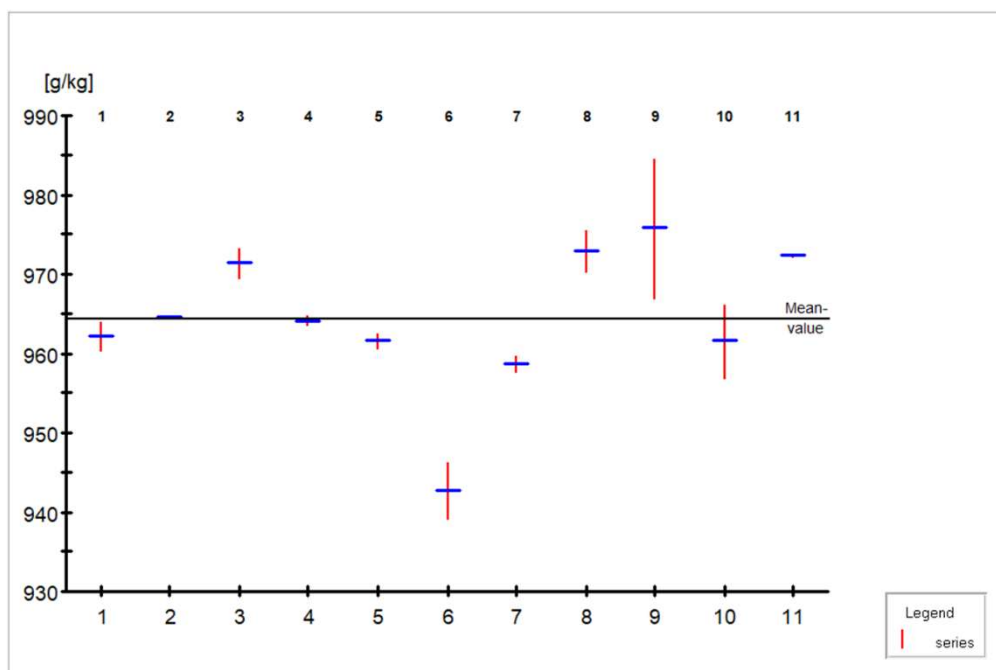
## Statistical summary (full set of 17 participants)

	Metribuzin TC_1	Metribuzin TC_2	Metribuzin WG 70	Metribuzin 70 % WG	Metribuzin WP 70	Metribuzin 70 % WP
$x_m$ [g/kg]	961.57	985.07	683.84	709.35	706.74	707.77
$x_m$ [% w/w]	96.16	98.51	68.38	70.94	70.67	70.78
L	17	17	17	17	17	17
$s_r$	6.15	8.24	7.97	3.99	5.80	4.58
$s_R$	12.51	13.66	17.39	7.52	10.10	7.35
r	17.22	23.07	22.32	11.17	16.23	12.83
R	35.02	38.26	48.69	21.04	28.28	20.58
$RSD_R$	1.30	1.39	2.54	1.06	1.43	1.04
$RSD_{R(Hor)}$	2.01	2.00	2.12	2.11	2.11	2.11
HorRat	0.65	0.70	1.20	0.50	0.68	0.49

## Statistical summary (full set of 17 participants)

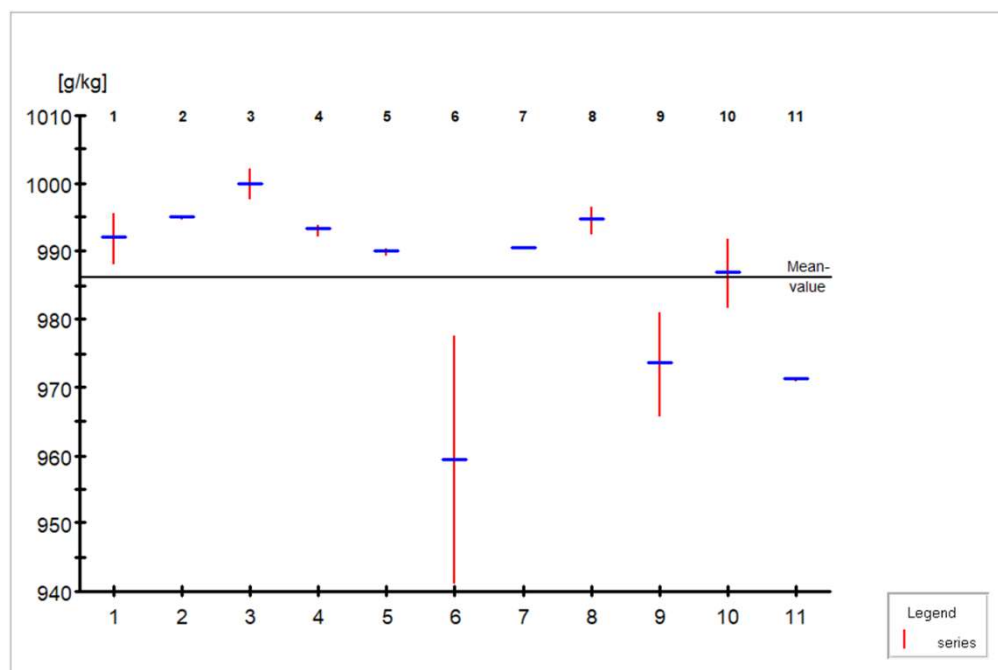
	Metribuzin SC 600 (522 g/kg Metribuzin)	Metribuzin SC 480 (414 g/kg Metribuzin)	Metribuzin 42 % SC
$x_m$ [g/kg]	529.25	414.87	428.81
$x_m$ [% w/w]	52.93	41.49	42.88
L	17	17	17
$s_r$	4.81	3.87	4.15
$s_R$	7.90	7.34	10.55
r	13.47	10.84	11.62
R	22.13	20.56	29.55
$RSD_R$	1.49	1.77	2.46
$RSD_{R(Hor)}$	2.20	2.28	2.27
HorRat	0.68	0.78	1.08

# Metribuzin TC\_1 (result of 11 laboratories who used Helium as carrier gas)



Mean value:	964.37 g/kg
$s_r$ :	4.74
$s_R$ :	9.77
$RSD_R$ :	1.01
$RSD_{R(Hor)}$ :	2.01
HorRat:	0.50
Outlier (Grubbs):	none
Straggler (Grubbs)	none

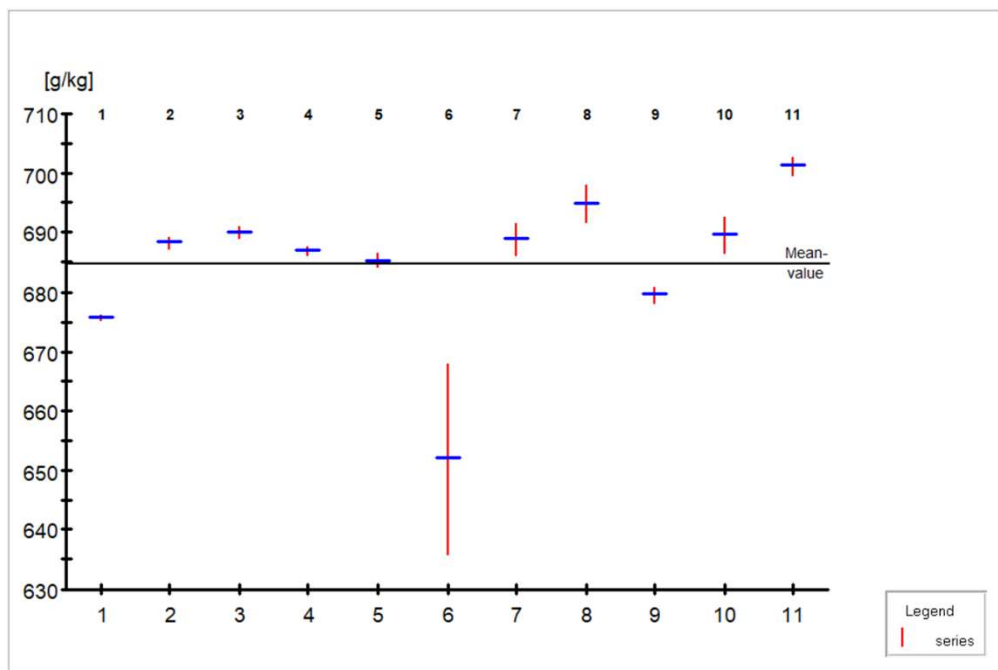
# Metribuzin TC\_2 (result of 11 laboratories who used Helium as carrier gas)



Mean value:	986.08 g/kg
$s_r$ :	8.80
$s_R$ :	13.92
$RSD_R$ :	1.41
$RSD_{R(Hor)}$ :	2.00
HorRat:	0.71
Outlier (Grubbs):	none
Straggler (Grubbs)	none

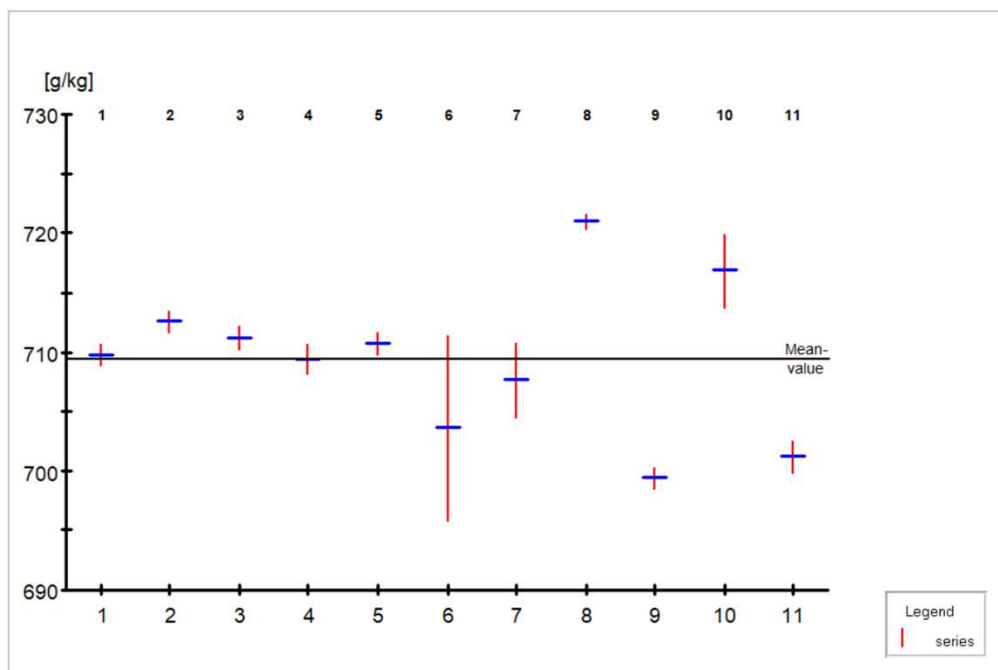


# Metribuzin WG 70 (result of 11 laboratories who used Helium as carrier gas)



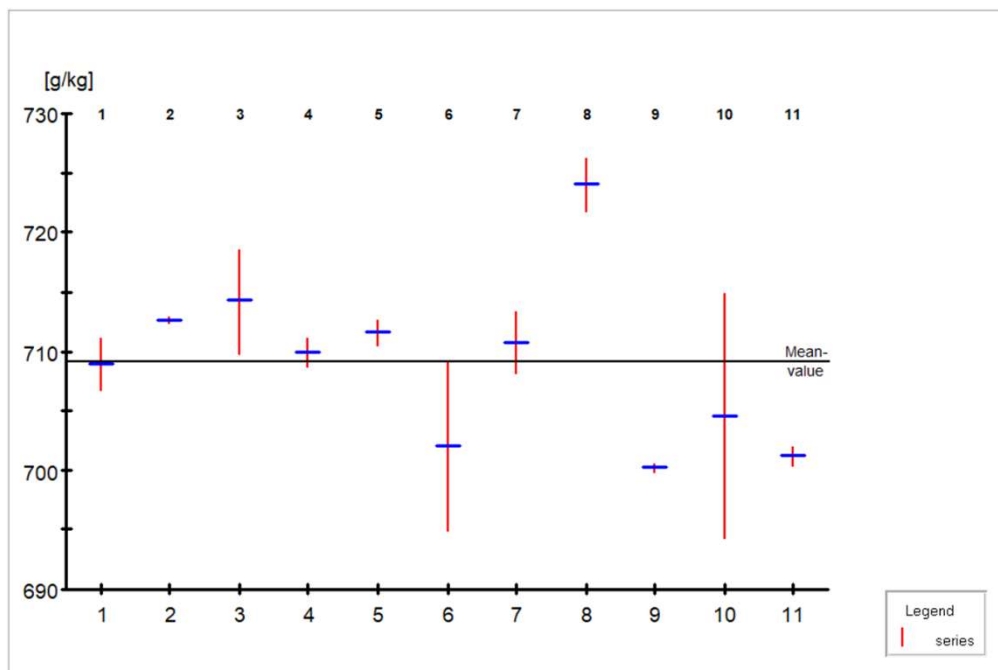
Mean value:	684.83 g/kg
s <sub>r</sub> :	7.16
S <sub>R</sub> :	13.77
RSD <sub>R</sub> :	2.01
RSD <sub>R (Hor)</sub> :	2.12
HorRat:	0.95
Outlier (Grubbs):	none
Straggler (Grubbs)	none

# Metribuzin 70 % WG (result of 11 laboratories who used Helium as carrier gas)



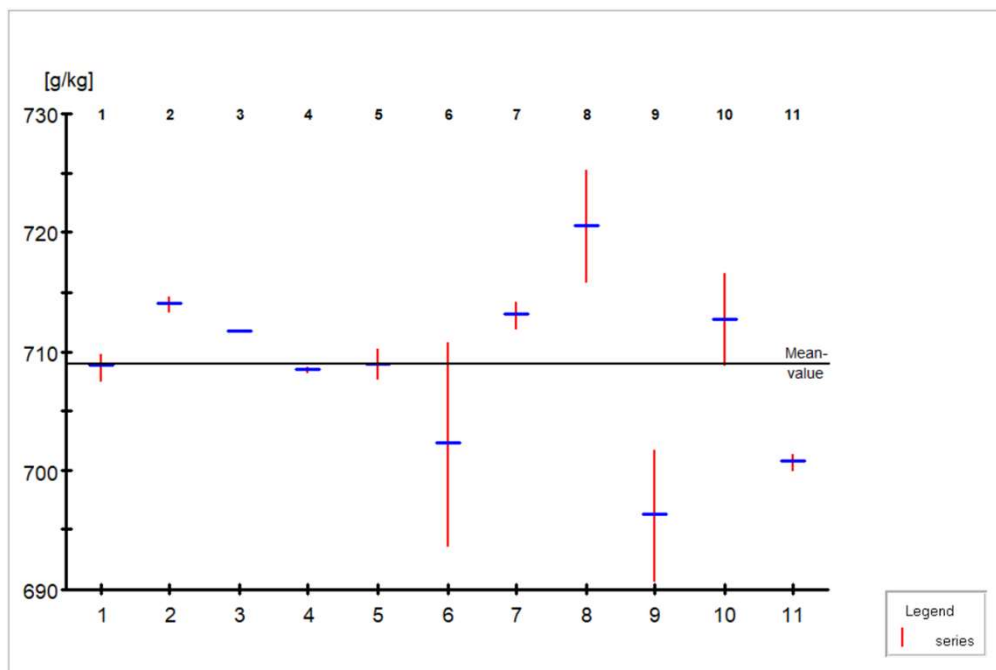
Mean value:	709.43 g/kg
s <sub>r</sub> :	3.95
s <sub>R</sub> :	6.98
RSD <sub>R</sub> :	0.98
RSD <sub>R (Hor)</sub> :	2.11
HorRat:	0.46
Outlier (Grubbs):	none
Straggler (Grubbs)	none

# Metribuzin WP 70 (result of 11 laboratories who used Helium as carrier gas)



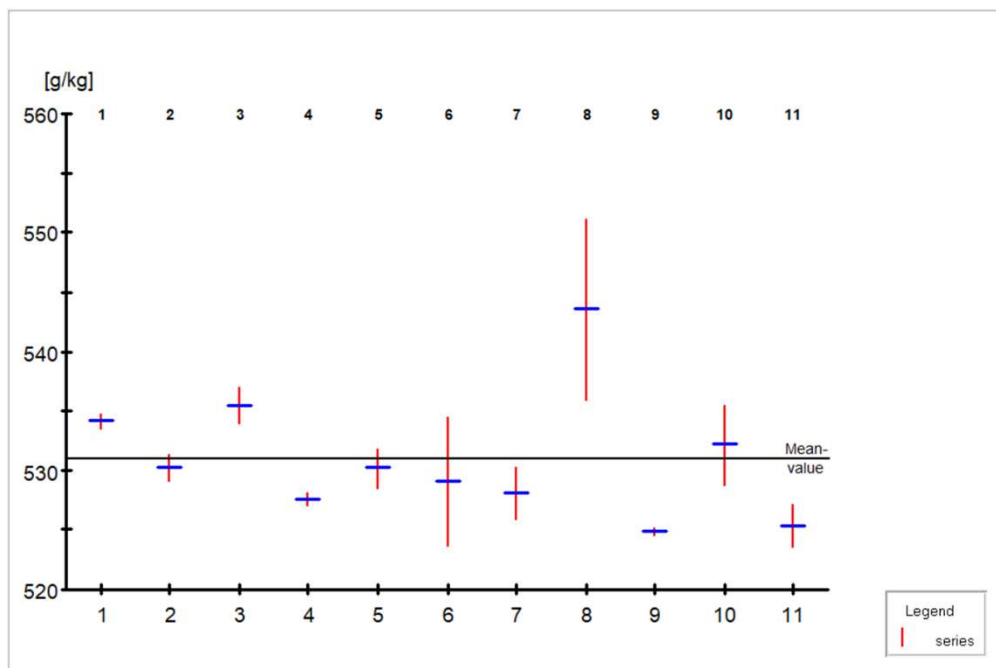
Mean value:	709.12 g/kg
$S_r$ :	5.89
$S_R$ :	8.10
$RSD_R$ :	1.14
$RSD_{R(Hor)}$ :	2.11
HorRat:	0.54
Outlier (Grubbs):	none
Straggler (Grubbs)	none

# Metribuzin 70 % WP (result of 11 laboratories who used Helium as carrier gas)



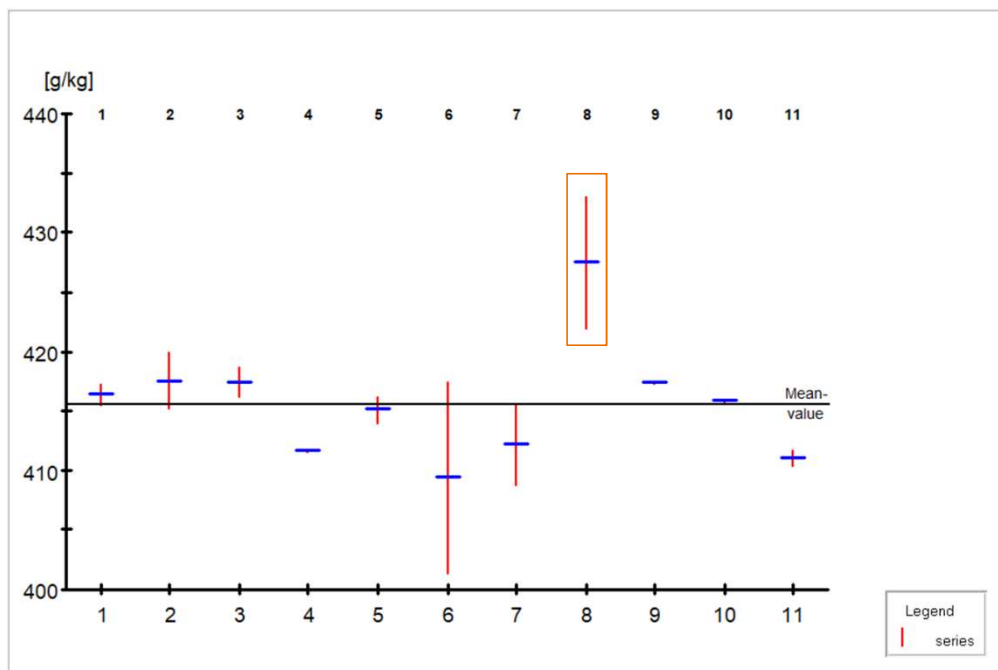
Mean value:	708.90 g/kg
s <sub>r</sub> :	5.06
s <sub>R</sub> :	7.75
RSD <sub>R</sub> :	1.09
RSD <sub>R (Hor)</sub> :	2.11
HorRat:	0.52
Outlier (Grubbs):	none
Straggler (Grubbs)	none

# Metribuzin SC 600 (result of 11 laboratories who used Helium as carrier gas)



Mean value:	531.01 g/kg
$S_r$ :	4.49
$S_R$ :	6.19
$RSD_R$ :	1.16
$RSD_{R(Hor)}$ :	2.20
HorRat:	0.53
Outlier (Grubbs):	none
Straggler (Grubbs)	none

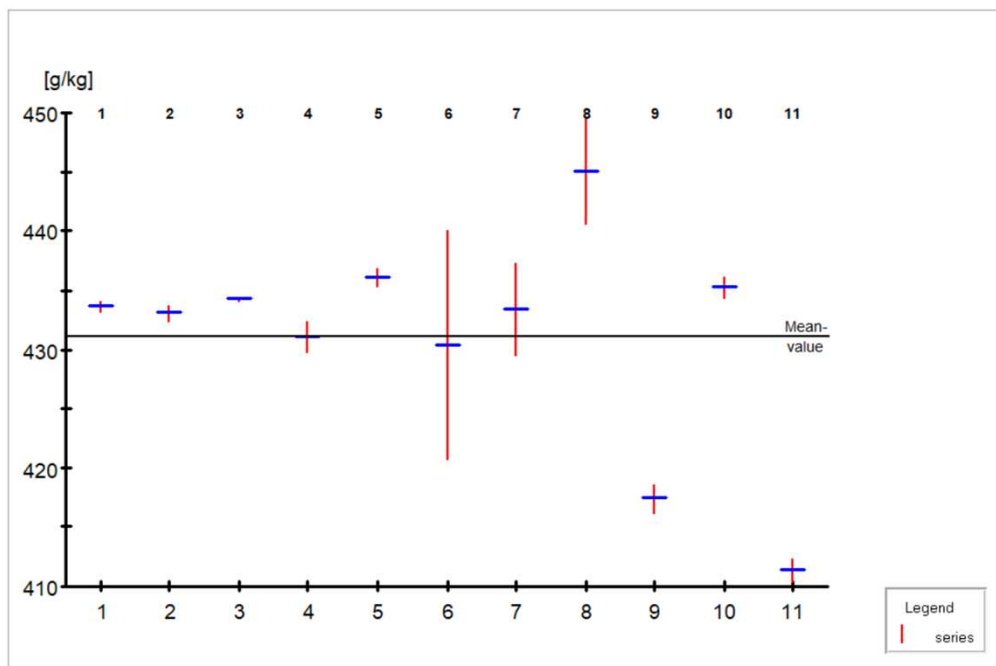
# Metribuzin SC 480 (result of 11 laboratories who used Helium as carrier gas)



Mean value:	415.61 g/kg
$s_r$ :	4.54
$s_R$ :	5.87
$RSD_R$ :	1.41
$RSD_{R(Hor)}$ :	2.28
HorRat:	0.62
Outlier (Grubbs):	none
Straggler (Grubbs)	upper (lab 8)*

\*refers to laboratory 9 in the list of all participants

# Metribuzin 42 % SC (result of 11 laboratories who used Helium as carrier gas)



Mean value:	431.02 g/kg
s <sub>r</sub> :	4.87
s <sub>R</sub> :	9.81
RSD <sub>R</sub> :	2.28
RSD <sub>R (Hor)</sub> :	2.27
HorRat:	1.00
Outlier (Grubbs):	none
Straggler (Grubbs)	none

# Statistical summary (result of 11 laboratories who used Helium as carrier gas)

	Metribuzin TC_1	Metribuzin TC_2	Metribuzin WG 70	Metribuzin 70 % WG	Metribuzin WP 70	Metribuzin 70 % WP
$x_m$ [g/kg]	964.37	986.08	684.83	709.43	709.12	708.90
$x_m$ [% w/w]	96.44	98.61	68.48	70.94	70.91	70.89
L	11	11	11	11	11	11
$s_r$	4.74	8.80	7.16	3.95	5.89	5.06
$s_R$	9.77	13.92	13.77	6.98	8.10	7.75
r	13.26	24.63	20.04	11.05	16.49	14.17
R	27.35	38.98	38.56	19.55	22.68	21.70
$RSD_R$	1.01	1.41	2.01	0.98	1.14	1.09
$RSD_{R(Hor)}$	2.01	2.00	2.12	2.11	2.11	2.11
HorRat	0.50	0.71	0.95	0.46	0.54	0.52



## Statistical summary (result of 11 laboratories who used Helium as carrier gas)

	Metribuzin SC 600 (522 g/kg Metribuzin)	Metribuzin SC 480 (414 g/kg Metribuzin)	Metribuzin 42 % SC
$x_m$ [g/kg]	531.01	415.61	431.02
$x_m$ [% w/w]	53.10	41.56	43.10
L	11	11	11
$s_r$	4.49	4.54	4.87
$s_R$	6.19	5.87	9.81
r	12.56	12.72	13.63
R	17.32	16.43	27.47
$RSD_R$	1.16	1.41	2.28
$RSD_{R(Hor)}$	2.20	2.28	2.27
HorRat	0.53	0.62	1.00

# Impact of the carrier gas onto the Horwitz Ratio (HorRat)

Sample	HorRat		
	full set of labs (17) <sup>1)</sup>	reduced set (11) <sup>2)</sup>	$\Delta$
Metribuzin TC_1	0.65	0.50	0.15
Metribuzin TC_2	0.70	0.71	- 0.01
Metribuzin WG 70	1.20	0.95	0.25
Metribuzin 70 %WG	0.50	0.46	0.04
Metribuzin WP 70	0.68	0.54	0.14
Metribuzin 70 % WP	0.49	0.52	- 0.03
Metribuzin SC 600	0.68	0.53	0.15
Metribuzin SC 480	0.78	0.62	0.14
Metribuzin 42 % SC	1.08	1.00	0.08

1) Use of carrier gas Helium, Hydrogen and Nitrogen

2) Use of carrier gas Helium (default)

# Conclusions

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- **A total of 17 different laboratories have participated in this full scale collaborative study.**
- **The statistical evaluation is reported on the one hand with 11 laboratories which used Helium as described in the CIPAC method and on the other hand with the full set of participants.**
- **Six of the total 17 laboratories used Hydrogen or Nitrogen, respectively, in deviation of the original method.**
- **The data presented in the statistical summary show that the use of Helium leads to HorRat values all within the required range. However, despite carrier gas variation, 7 of 9 samples fulfilled the HorRat criterion, only two failed shortly.**
- **This is evidence that the present method is acceptable and robust and therefore is suitable to produce accurate and reproducible results.**

## Overall Conclusion

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Bayer AG, Crop Science Division and Jiangsu Seven Continent consider this method to be suitable for the intended purpose

**Bayer AG, Crop Science Division and Jiangsu Seven Continent recommend this method accepting it as a provisional CIPAC method for the determination of Metribuzin in technical material and in SC, WG and WG formulations**