Spinetoram

CIPAC 5250/R

Large Scale Collaborative Trial

Large scale collaborative study for CIPAC method for Spinetoram TC, SC, WG, and DT.

By

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1. **Introduction**

A large scale collaborative trial for CIPAC 802 Spinetoram was conducted to assess the performance of the analytical method for four Spinetoram formulation types: Technical (TC), Suspension Concentrate (SC), Water dispersible granules (WG), and a Direct Application Tablet (DT). Spinetoram is the sum of 2 separate molecules; Spinetoram-J (XDE-175-J) and Spinetoram-L (XDE-175-L).

This large-scale trial, supported by ESPAC, utilized 11 different laboratories which analyzed two separate batches of the TC and SC, and single batches of the WG and DT formulation types, these will be referenced as TC1, TC2, SC1, SC2, WG, and DT throughout this report. Of the 11 laboratories that participated, one laboratory was found to be an outlier in the analysis of DT and one lab an outlier in the analysis of the SC2.
The data provided was then analyzed to determine repeatability and reproducibility for each formulation type. To further support the robustness of the method, the Horwitz ratio was applied for each batch.
Based upon the consistency of the data generated, and the acceptable values found with the Horwitz equation, it is determined that the large-scale collaborative trial has proven this methodology to be robust and adequate in performance for the analysis of TC, SC, WG, and DT formulation types for Spinetoram. A proposal to CIPAC to accept this as a provisional method for Spinetoram is made.

2. **Method Description**

Spinetoram CIPAC 5249/m analytical method for TC and SC, WG and DT formulations

Outline of CIPAC Method: Spinetoram is determined by reversed phase high performance liquid chromatography (HPLC) using UV detection at 250nm and external standardization.

Reagents

Spinetoram reference standard with known Spinetoram-J and Spinetoram-L purities

Water HPLC Grade

Acetonitrile HPLC Grade

Methanol HPLC Grade

Buffer pH 5.5, 2g/L Ammonium Acetate in water

Solvent Mix A Acetonitrile – Methanol 80 + 20 (v/v)

Eluent Solvent Mix A – Buffer pH 5.5 80 + 20 (v/v)[1]

Calibration Solution Weigh in duplicate (to the nearest 0.1mg) about 43mg of the Spinetoram standard (s mg) into separate volumetric flasks (100mL). Add water (about 10mL) and swirl briefly to disperse. Add methanol (50mL) and shake to dissolve. Adjust to mark with methanol and mix well (Solutions C_1 and C_2).

Apparatus

High performance liquid chromatograph equipped with an ultraviolet spectrophotometric detector and an injection system capable to inject 10µL

Column Phenomenex Luna C8(2) 3µ 150x4.6mm, or equivalent material with the same selectivity

Electronic Integrator

Mechanical Shaker

Disposable filters, solvent compatible, porosity 0.45µm Nylon

Procedure

a. *Chromatographic Conditions (typical)*

Parameter	Specification
Column Temperature	30 ºC
Flow Rate	1.0 mL/min
Measuring Wavelength	250 nm
Injection Volume	10 µL

[1] If mixed online this ratio is equivalent to Acetonitrile – Methanol – Buffer 64 + 16 + 20 (v/v/v)

Run Time	Approx. 20min
Retention Time	Spinetoram-J: 10- 12min Spinetoram-L: 12-15min

b. *Equilibration of the system*
Pump sufficient eluent through the column to equilibrate the system. Inject 10µL portions of the calibration solution C_1 and repeat the injections until retention times and peak areas vary by less than ±0.5% of the mean for three successive injections.

c. Sample preparation (TC, SC, WG)
Weigh accurately, to the nearest 0.1 mg, sufficient sample to contain about 40mg spinetoram into a 100 mL volumetric flask. Add 10.0 mL of purified water with a volumetric pipette and briefly swirl sample to disperse. Add 50 mL of methanol and shake to dissolve. Adjust to 100.0mls with Methanol. Filter through a 0.45 µm nylon syringe filter for LC analysis, taking care to discard to waste the first few filtered drops.

d. Sample Preparation (DT)

For this collaborative study a total of around 100 tablets were ground in the Clarke laboratories and sub-samples of this milled material was supplied to each participating laboratory. For analysis of production or market samples at least 5 tablets from each batch should be milled or ground and then sub-samples taken for analysis as described below.

Weigh accurately, to the nearest 0.1 mg, sufficient sample of ground tablet to contain about 10 mg spinetoram into a 25 mL volumetric flask. Add 2.5 mL of purified water with a volumetric pipette and briefly swirl sample to disperse. Add 15 mL of methanol and shake to dissolve. Adjust to 25.0mls with Methanol. Filter through a 0.45 µm nylon syringe filter for LC analysis, taking care to discard to waste the first few filtered drops.

e. Determination
Inject 10µL portions of the calibration solutions (C_1 and C_2) and of the sample solutions (S_1, S_2, …, etc.) in the following sequence:
C_1, S_1, C_2, S_2, …
Determine the peak area of each Spinetoram component (Spinetoram-J and Spinetoram-L) and calculate the response factors (*f*) from the calibration solutions bracketing the injections of the sample solutions. Average the response factors of the calibration solutions preceding and following the sample solution injections. The results for each individual component **must** be calculated separately and then added together for the total Spinetoram content. Do not add the areas together first.

f. Calculations

Amount Spinetoram-J or Spinetoram-L (mg) = $W_a \times P$

Where*:*
W_a = weight of respective component in calibration solution
P = Purity, decimal

RF = Amount Spinetoram* ÷ Area Spinetoram*

Where:
RF = Response factor for respective component J or L
*Amount Spinetoram** = calculated amount of respective J or L component (mg) in calibration solution
*Area Spinetoram** = Peak area for respective J or L component in calibration solution

Weight % = Area Spinetoram* × RF ÷ S × 100%
Where:
Weight % = Weight % of respective J or L component
*Area Spinetoram** = Peak area of respective J or L component in sample solution
RF = Response factor calculated for respective J or L component
S = Sample weight, mg
The total amount of Spinetoram is the sum of the weight % of Spinetoram-J and Spinetoram-L.

3. **Method Assessment**

According to the CIPAC guidelines for collaborative study procedures for assessment of performance of analytical methods, CIPAC 5249/m Spinetoram was investigated.

Four formulation types, TC, SC, WG, and DT, were utilized in the study. For formulation types, TC and SC, there were two separate batches and single batches only for the WG and DT, giving a total of six separate samples. Each batch was prepared in duplicate on two separate days, for a total of 8 data points per batch. Originally there were 18 labs that accepted to participate. Unfortunately, due to shipping challenges, only a total of 11 labs received the samples safely and provided the appropriate data by the due date.
The nominal concentration of spinetoram in the material were the following:
-Technical material (TC): 858g/kg
-Suspension concentration (SC): 120g/L (117 g/kg)
-Water dispersible (WG): 250 g/kg
-Direct application to water (DT): 10 g/kg

The following laboratories participated in the large-scale collaborative trial, and are in no particular order with the results that are provided in the report:

Laboratory
Benaki Phytopathological Institute 8 Stefanou Delta Street, 14561, Kifissia, Athens Greece
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
National Phytosanitary Authority Voluntari Bvd. No. 11, Voluntari Town, Ilfov County, Romania
Alchimex SA 63-Alexandru Constantinescu-011472 Bucharest-1 Romania
Maryland Department of Agriculture 50 Harry S Truman Parkway Annapolis, MD 21401
Clarke International LLC 675 Sidwell Court St. Charles, IL 60174
The Pesticide Control Laboratory, Backweston Laboratory Complex, Backweston, Celbridge, Co. Kildare Ireland
BASF SE RAA/AC - E210 Dr. Rolf Foerster Carl-Bosch-Strasse 38 D-67056 Ludwigshafen GERMANY
Frandesa Co., Ltd 1, Bereza District, 225209 Brest Region, Republic of Belarus

Laboratory
Walloon Agricultural Research Centre (CRA-W) Agriculture and Natural Environment Department (D3) Plant Protection Products and Biocides Physico-chemistry and Residues Unit (U10) Carson Building Rue du Bordia, 11 B-5030 GEMBLOUX BELGIUM
Laboratorio de Formulaciones de Plaguicidas División Análisis y Diagnóstico Dirección General de Servicios Agrícolas Ministerio de Ganadería Agricultura y Pesca Avenida Millán 4703 esq. Vedia C.P.:12900 Montevideo Uruguay

a. **Individual Laboratory Results**

Each laboratory generated 8 results per formulation per batch.

TC1												
Lab	1	2	3	4	5	6	7	8	9	10	11	
Spinetoram Content (wt.%)	87.1	89.3	94.4	89.5	92.6	89.5	89.7	90.0	90.7	89.3	85.8	Day 1
	86.4	89.0	94.6	88.9	90.6	88.9	89.7	90.0	90.6	89.4	85.9	
	87.5	89.1	95.6	90.3	91.8	90.3	86.9	90.2	90.7	89.4	85.4	
	87.9	88.6	95.2	89.2	91.9	89.2	87.3	90.1	90.6	89.2	85.7	
	88.8	90.4	94.0	89.7	91.2	87.6	90.6	89.2	89.6	91.4	85.3	Day 2
	88.8	90.1	91.7	89.7	89.6	89.5	91.2	89.3	89.6	91.4	85.4	
	89.0	90.5	93.8	90.1	91.4	88.6	91.9	90.0	89.5	92.0	85.4	
	88.9	90.2	94.1	89.0	90.3	88.2	91.8	90.1	89.7	92.1	85.6	
Average	88.1	89.7	94.2	89.6	91.18	89.0	89.9	89.9	90.1	90.5	85.6	

TC2												
Lab	1	2	3	4	5	6	7	8	9	10	11	
Spinetoram Content (wt.%)	89.1	89.0	93.7	87.70	89.8	87.7	79.8	90.6	90.4	90.2	85.9	Day 1
	88.1	89.1	91.4	89.50	91.5	89.5	80.0	90.5	90.5	90.1	85.8	
	89.4	90.5	91.0	89.40	91.1	89.4	85.3	90.2	90.4	90.0	85.8	
	89.4	89.2	90.9	88.00	89.8	88.0	85.2	90.1	90.5	90.0	85.8	
	89.9	90.8	94.0	87.60	90.9	87.6	92.3	90.7	90.8	92.2	85.5	Day 2
	89.9	90.6	91.7	89.50	92.7	89.5	91.9	90.5	90.9	92.2	85.9	
	87.2	90.4	93.8	88.60	90.6	88.6	92.2	90.6	90.8	92.2	85.4	
	87.0	90.3	94.1	88.20	91.4	88.2	92.3	90.5	90.5	92.2	85.9	
Average	88.8	90.0	92.6	88.56	91.0	88.6	87.4	90.5	90.6	91.1	85.8	

SC1												
Lab	1	2	3	4	5	6	7	8	9	10	11	
Spinetoram Content (wt.%)	11.9	11.9	12.1	11.7	11.8	11.7	12.2	12.1	12.1	12.1	12.0	Day 1
	11.9	12.2	12.1	11.7	11.9	11.7	12.1	12.1	12.1	12.1	12.0	
	11.9	11.9	12.5	11.6	11.5	11.6	10.8	12.1	12.1	12.1	12.0	
	11.9	11.9	12.1	11.7	11.7	11.7	10.8	12.1	12.1	12.1	12.0	
	12.0	12.2	12.5	11.6	11.5	11.6	12.3	12.0	12.3	12.4	12.0	Day 2
	12.0	12.2	12.2	11.5	11.3	11.5	12.3	12.0	12.3	12.4	12.0	
	12.1	12.0	12.0	11.7	11.6	11.7	12.3	12.0	12.3	12.4	12.0	
	12.1	12.0	12.0	11.8	11.8	11.8	12.2	12.0	12.4	12.4	12.0	
Average	12.0	12.0	12.2	11.7	11.6	11.7	11.9	12.1	12.2	12.3	12.0	

SC2												
Lab	1	2	3	4	5	6	7	8	9	10	11	
Spinetoram Content (wt.%)	14.1	12.7	12.7	12.7	12.6	12.7	12.3	12.8	12.9	13.0	12.0	Day 1
	14.0	12.7	12.7	12.5	12.4	12.5	12.2	12.8	12.9	13.0	12.0	
	14.4	12.7	12.8	12.7	12.3	12.7	12.2	12.7	12.9	13.1	12.8	
	14.4	12.7	13.1	12.7	12.6	12.7	12.3	12.7	12.9	13.1	12.8	
	13.6	12.6	13.0	12.8	12.6	12.8	13.0	12.6	13.2	13.3	12.6	Day 2
	13.6	12.7	13.0	12.7	12.5	12.7	13.0	12.6	13.3	13.5	12.4	
	13.8	12.7	12.7	12.9	12.4	12.9	13.0	12.6	13.2	13.4	12.5	
	13.7	12.7	12.8	12.9	12.2	12.9	13.0	12.6	13.3	13.5	12.9	
Average	14.0	12.7	12.9	12.7	12.5	12.7	12.6	12.7	13.1	13.2	12.5	

WG												
Lab	1	2	3	4	5	6	7	8	9	10	11	
Spinetoram Content (wt.%)	24.6	24.3	25.3	24.1	24.6	24.1	24.6	24.4	24.5	24.3	25.2	Day 1
	24.5	24.3	24.6	23.7	24.3	23.7	24.6	24.4	24.5	24.3	25.4	
	24.6	24.3	25.2	24.0	24.4	24.0	24.4	24.4	24.4	24.4	25.2	
	24.6	24.2	25.2	23.9	24.0	23.9	24.4	24.4	24.5	24.3	25.2	
	23.8	24.3	24.4	24.3	24.1	24.3	25.0	23.9	24.9	25.1	25.2	Day 2
	23.8	24.2	25.0	24.3	24.6	24.3	24.9	24.0	25.0	25.1	25.2	
	24.4	24.4	25.2	24.3	24.3	24.3	25.0	24.2	24.9	25.1	24.9	
	24.4	24.5	25.2	23.7	24.6	23.7	25.0	24.2	24.9	25.2	25.0	
Average	24.3	24.3	25.0	24.0	24.4	24.0	24.7	24.2	24.7	24.7	25.2	

DT												
Lab	1	2	3	4	5	6	7	8	9	10	11	
Spinetoram Content (wt.%)	1.06	0.961	0.978	0.971	0.664	0.971	1.02	1.01	1.01	0.984	0.254	Day 1
	1.05	0.971	0.954	0.958	0.678	0.958	1.02	1.01	1.01	0.985	0.254	
	1.04	0.986	0.952	0.951	0.924	0.951	1.02	1.00	0.998	0.981	0.252	
	1.04	0.984	0.974	0.971	0.927	0.971	1.01	1.00	0.997	0.982	0.254	
	0.982	1.01	0.968	0.982	0.926	0.982	0.966	0.658	1.02	0.972	0.326	Day 2
	0.982	1.00	0.944	0.982	0.921	0.982	0.968	0.658	1.01	0.982	0.324	
	0.983	0.986	0.946	0.940	0.953	0.940	0.938	0.769	1.01	1.01	0.250	
	0.986	0.989	0.970	0.930	0.934	0.930	0.937	0.769	1.02	1.01	0.250	
Average	1.02	0.986	0.961	0.961	0.866	0.961	0.985	0.859	1.01	0.988	0.271	

All statistical analysis was performed using the average values for each lab.

b. **Determine any outliers**

The Grubbs' Test was utilized to determine whether any of the data points was considered a straggler or an outlier. The critical values used were for p = 11. This put the upper 1% value at 2.485 and the upper 5% value at 2.234. Both the largest and smallest value was tested, utilizing the average results for each lab for each respective formulation type and batch.

Means	Level j											
Lab (i)	TC1		TC2		SC1		SC2		WG		DT	
	y_{ij}	n_{ij}	y_{ij}	n_{ij}	y_{ij}	n_{ij}	y_{ij}	n_{ij}	y_{ij}	n_{ij}	y_{ij}	n_{ij}
1	88.05	8	88.75	8	11.98	8	13.95	8	24.34	8	1.02	8
2	89.65	8	89.99	8	12.04	8	12.69	8	24.31	8	0.99	8
3	94.18	8	92.58	8	12.19	8	12.85	8	25.01	8	0.96	8
4	89.55	8	88.56	8	11.66	8	12.74	8	24.04	8	0.96	8
5	91.18	8	90.98	8	11.64	8	12.45	8	24.36	8	0.87	8
6	88.98	8	88.56	8	11.66	8	12.74	8	24.04	8	0.96	8
7	89.89	8	87.38	8	11.88	8	12.63	8	24.74	8	0.98	8
8	89.86	8	90.46	8	12.05	8	12.68	8	24.24	8	0.86	8
9	90.13	8	90.60	8	12.21	8	13.08	8	24.70	8	1.01	8
10	90.53	8	91.14	8	12.25	8	13.24	8	24.73	8	0.99	8
11	85.56	8	85.75	8	12.00	8	12.50	8	25.16	8	0.27	8

The maximum value was an outlier, which was identified in Lab 1 for SC2. The minimum value was an outlier, which was identified in Lab 11 for the DT.

Upper 1%	2.485	Upper 5%	2.234			
	TC1	TC2	SC1	SC2	WG	DT
Lowest value	85.56	85.75	11.64	12.45	24.04	0.27
Highest value	94.18	92.58	12.25	13.95	25.16	1.02
G_1 (smallest value)	2.021	1.946	1.433	0.974	1.265	2.926
G_p (largest value)	2.110	1.575	1.296	2.539	1.717	0.556

Grubbs statistic values were compared to the upper 1% and 5% values. If the Grubbs statistic was ≤ 5% critical value, the result in question was accepted. If the statistic was ≥ 5% critical value and ≤ 1% critical value, then the result in question was considered a straggler. If the statistic was > 1% critical value, the result in question was considered an outlier. Using data from all 11 labs then DT results for lab 11 was an outlier and SC2 for lab 1 was an outlier.

Removing both lab 11 (DT) and lab 1 (SC2) and rechecking for outliers showed no stragglers or outliers remaining.

Upper 1%	2.41	Upper 5%	2.176			
	TC1	TC2	SC1	SC2	WG	DT
Lowest value	85.56	85.75	11.64	12.45	24.04	0.86
Highest value	94.18	92.58	12.25	13.24	25.16	1.02
G_1 (smallest value)	2.021	1.946	1.433	1.266	1.265	1.837
G_p (largest value)	2.110	1.575	1.296	1.977	1.717	1.035

c. **Determine the Repeatability**

Repeatability was determined using the average results for each lab for each batch of material. Analysis was performed per ISO 5725-2 1994 section 7.4.5.1. Based on the results from the Grubbs' test, Lab 1 for SC2 and Lab 11 for DT were not included in the statistical analysis. Repeatability was determined as repeatability variance * 2.8.

The repeatability data is summarized below:

	TC1 and TC2 average at	SC1 and SC2 at nominal	WG at nominal 250 g/kg	DT at nominal 10 g/kg

Repeatability, r	47.6	7.35	9.02	2.12

d. **Determine the Reproducibility**

Reproducibility was determined using the average result for each lab for each batch of material. Analysis was performed per ISO 5725-2 1994 section 7.4.5.2. Based off the results from the Grubbs' test, Lab 1 for SC2 and Lab 11 for DT were not included in the statistical analysis. Reproducibility was determined as reproducibility variance * 2.8.

The reproducibility data is summarized below:

	TC1 and TC2 average at	SC1 and SC2 at nominal	WG at nominal 250 g/kg	DT at nominal 10 g/kg
Repeatability, r	72.8	9.51	13.52	2.50

e. **Application of the Horwitz Equation**

The Horwitz equation is defined as follows:
$\%RSD = 2^{(1-0.5*\log(C))}$
C = concentration of analyte expressed as a decimal.

The ratio between the %RSD of the results and the %RSD from the Horwitz equation provides a value known as the Horwitz ratio. This ratio can be indicative of the repeatability of a method and whether the results can be seen as acceptable or not. The following criteria is generally accepted as the interpretation of the Horwitz Ratio.

Horwitz Ratio Range	**Acceptability**
$0.3 \leq \text{Ratio} \leq 1$	Acceptable
$\text{Ratio} < 0.3$ or $1 < \text{Ratio} \leq 2$	Acceptable but may require explanation
$\text{Ratio} > 2$	Not acceptable

Applying this criteria we can determine that all four samples had acceptable ratios. For SC2 and DT, as with the previous statistical analyses, Lab 1 and 11 were excluded as they were considered as outliers.

Sample	TC1	TC2	SC1	SC2	WG	DT
%RSD	2.32	2.17	1.88	1.90	1.54	5.67
%RSD Horwitz equation	2.03	2.03	2.75	2.73	2.47	4.03
Horwitz Ratio	1.1	1.1	0.7	0.7	0.6	1.4

The results for TC samples (1.1) were slightly above the normally acceptable tolerance range ($0.3 \leq \text{Ratio} \leq 1$) but this may be due to nature of this technical material (a mixture of 2 main factors and a technical process which involves a biological fermentation step). The Horowitz ratio for the DT (1.4) is also outside the normally acceptable range and this may be due to the fact that the DT is a heterogenous formulation with very low active ingredient content (10 g/kg nominal).

Using the data generated and the calculated Horwitz ratio, we propose that the data supports the robustness of this method for both TC, SC,WG and DT formulations.

4. **Participant Comments and Deviations from Proposed Method**

The following is a summary of any comments made by the participating labs, as well as highlighting any deviations or differences from the proposed methodology.

Lab	Deviations
1	Different column was used: ZORBAX SB-C8 4.6x150mm 3.5µm
2	None
3	Different column was used: Gemini NX – C18 3µm, 100 x 4.6 mm
4	Different column was used: Phenomenex Luna 3um C18(2) 100x3mm
5	None
6	Different column was used: Phenomenex Luna 3um C18(2) 100x3mm
7	None
8	None
9	Different column was used: Phemonenex Kinetex CoreShell-C18 150x4.6mm 5um

10	None
11	Slightly different column used: phenomenex luna C8 5u 150x4,6mm

Most deviations were related to the column utilized in the analysis. Based on the statistical analysis, the modification of the column had no significant impact on the results.

5. Conclusion

This large-scale collaborative trial for Spinetoram was completed by 11 separate laboratories, analyzing two separate batches of TC and two separate batches of SC, over two days. Along with one batch of the WG and DT, over two days. The average result from each laboratory for each batch of formulation was utilized in statistical analysis to determine the repeatability, reproducibility as well as determine the Horwitz ratio to aid in determining method acceptability. Based upon the Grubbs' test for outliers, Laboratory 1 and 11 were an outlier in two batches (SC2 and DT respectively)

After removal of the two outliers the repeatability for the TC, SC, WG, and DT formulations were determined to be, respectively, 4.76 wt% (47.6 g/kg), 0.735 wt% (7.4 g/kg), 0.903 wt% (9.0 g/kg), 0.212 wt% (2.1 g/kg). The reproducibility for the TC, SC, WG, and DT formulations were determined to be, respectively, 7.28 wt% (72.8 g/kg), 0.951 wt% (9.5 g/kg), 1.35 wt% (13.5 g/kg), 0.25 wt% (2.5 g/kg).

The Horwitz ratio was used to assist in the acceptability of the methodology. The ratios for TC1, TC2, SC1, SC2, WG, and DT were 1.1, 1.1, 0.7, 0.7, 0.6 and 1.4, respectively. For acceptability of these values, the range is $\geq$ 0.3 and $\leq$ 1.0. For the DT, even though it was just outside the "acceptable" range, it is deemed acceptable due to the material having a low-level concentration and has a heterogenous nature, but a 1.4 ratio gives no final difference of concentration. In addition, for the TC being very slightly above the "acceptable" range, this is due to many co-excipients with the product production process being a fermentation process. In conclusion, bearing in mind the complexities of the spinetoram products described, is robust and provides acceptable performance for Spinetoram TC, SC, WG and DT formulations.

It was noted that different column types were used across many labs, with no major impact of the results, but that the Luna C(8) column should be used for the final method.

Overall, it was deemed the large-scale trial was successful and produced consistent, repeatable and reproducible results. We propose that this method is accepted as provisional by CIPAC.

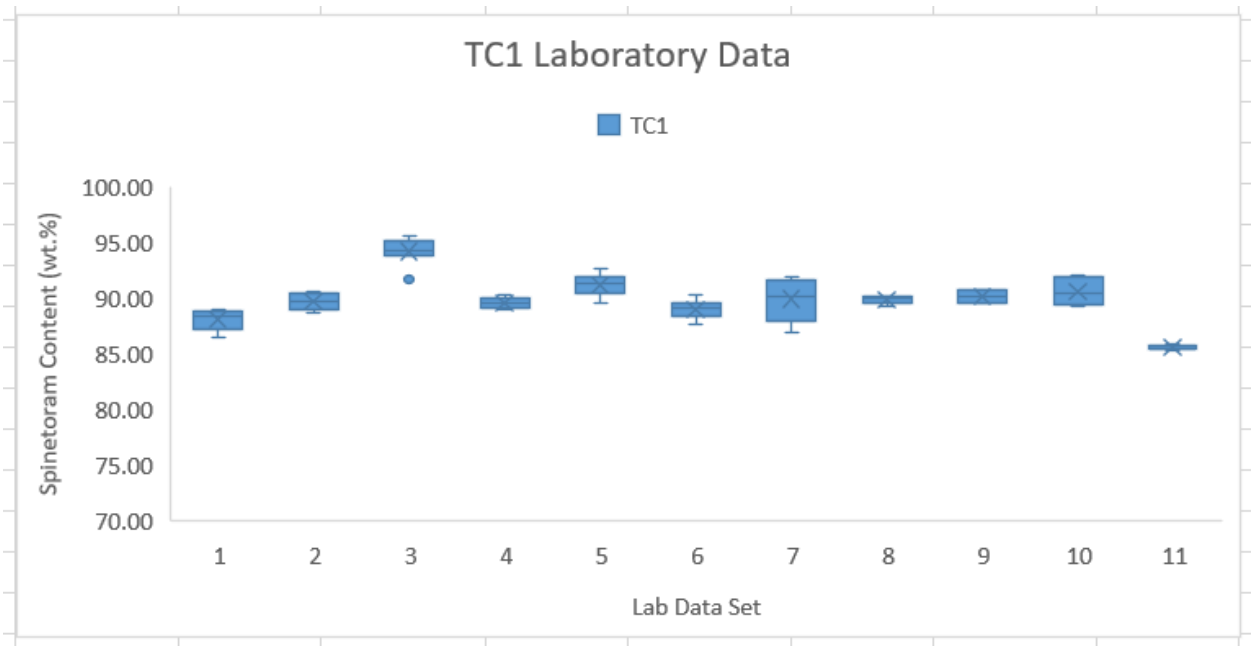
Appendix I – Collaborative Study Presentation of Results

Statistical variable	TC1	TC2	SC1	SC2	WG	DT
X	89.8	89.5	12.0	12.8	24.5	0.959
L	11	11	11	10	11	10
S_r	1.18	2.22	0.283	0.243	0.322	0.076
S_L	2.04	1.77	0.201	0.227	0.360	0.047
S_R	2.36	2.84	0.347	0.333	0.483	0.089
RSD_r	1.31	2.48	2.36	1.90	1.32	7.90
RSD_R	2.63	3.18	2.90	2.61	1.97	9.31
r	3.29	6.23	0.791	0.680	0.903	0.212
R	6.60	7.96	0.971	0.931	1.35	0.25
RSD_R(Hor)	2.03	2.03	2.75	2.73	2.47	4.03

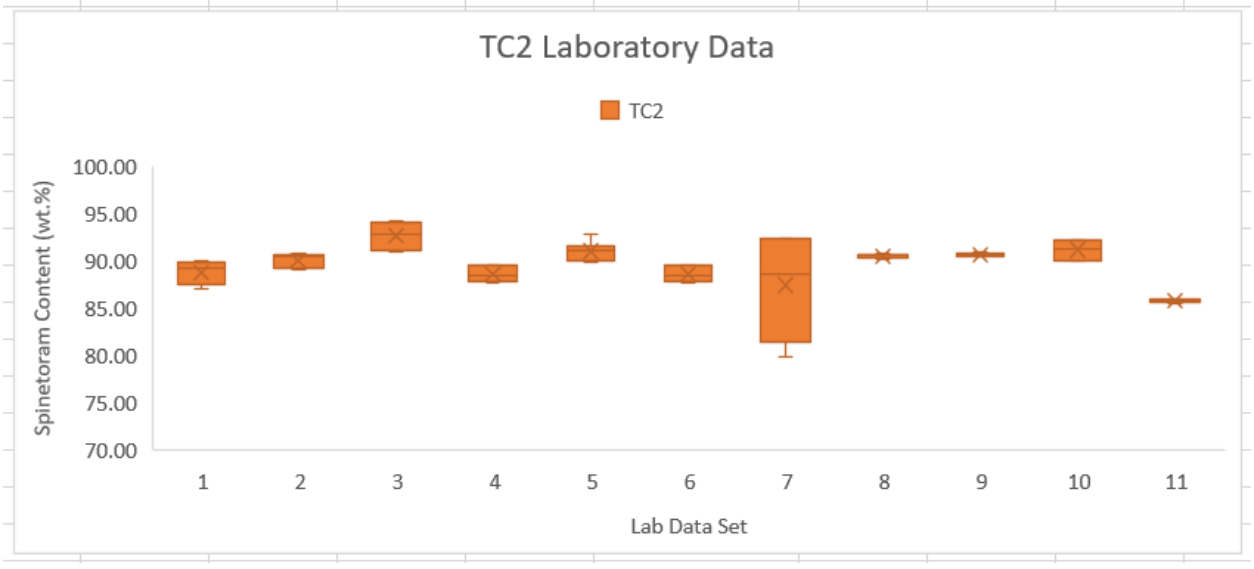
Where:

X = average
L = number of laboratories
S_r = repeatability standard deviation
S_L = “pure” between laboratory standard deviation
S_R = reproducibility standard deviation
RSD_r = repeatability relative standard deviation
RSD_R = reproducibility relative standard deviation
r = repeatability
R = reproducibility
RSD_R(Hor) = Horwitz value

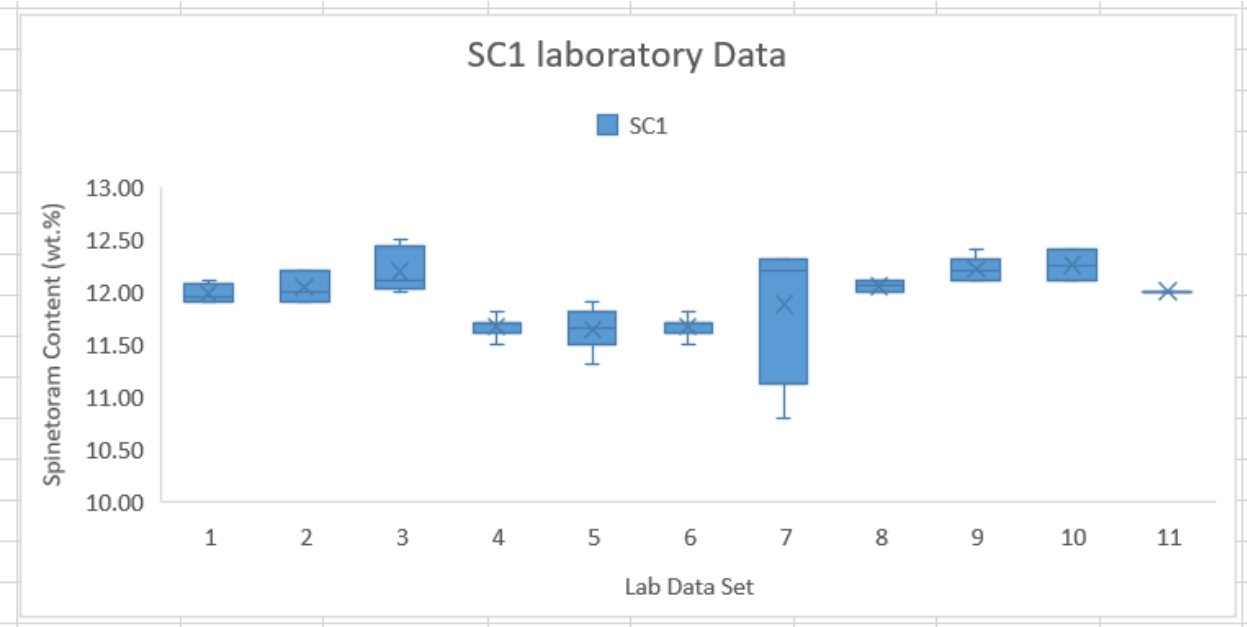
Appendix II – TC1 Statistical Bar Chart



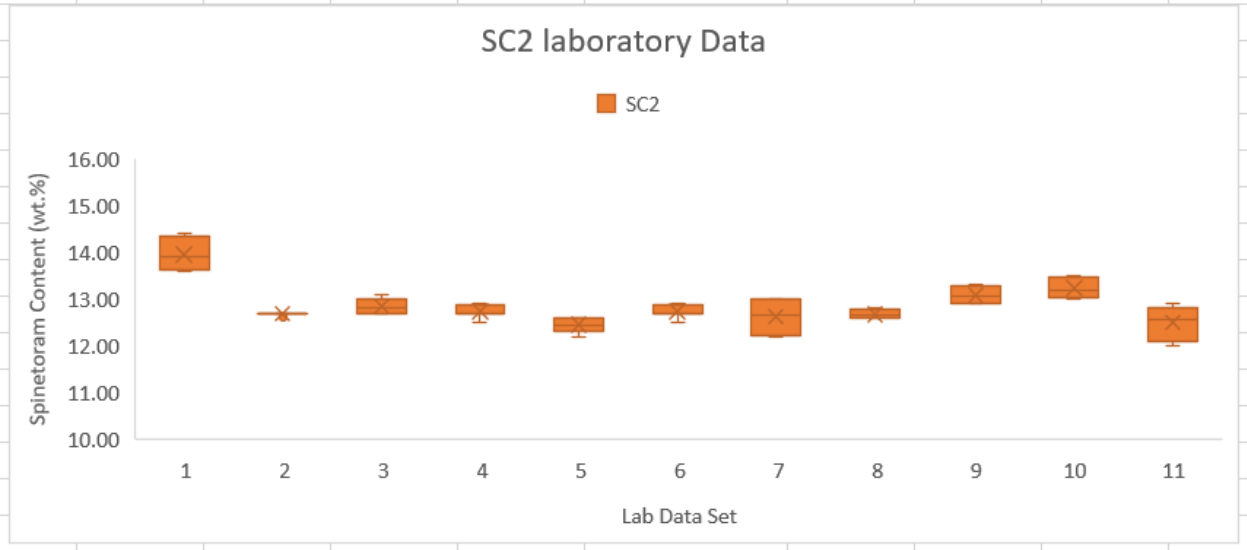
Appendix III – TC2 Statistical Bar Chart



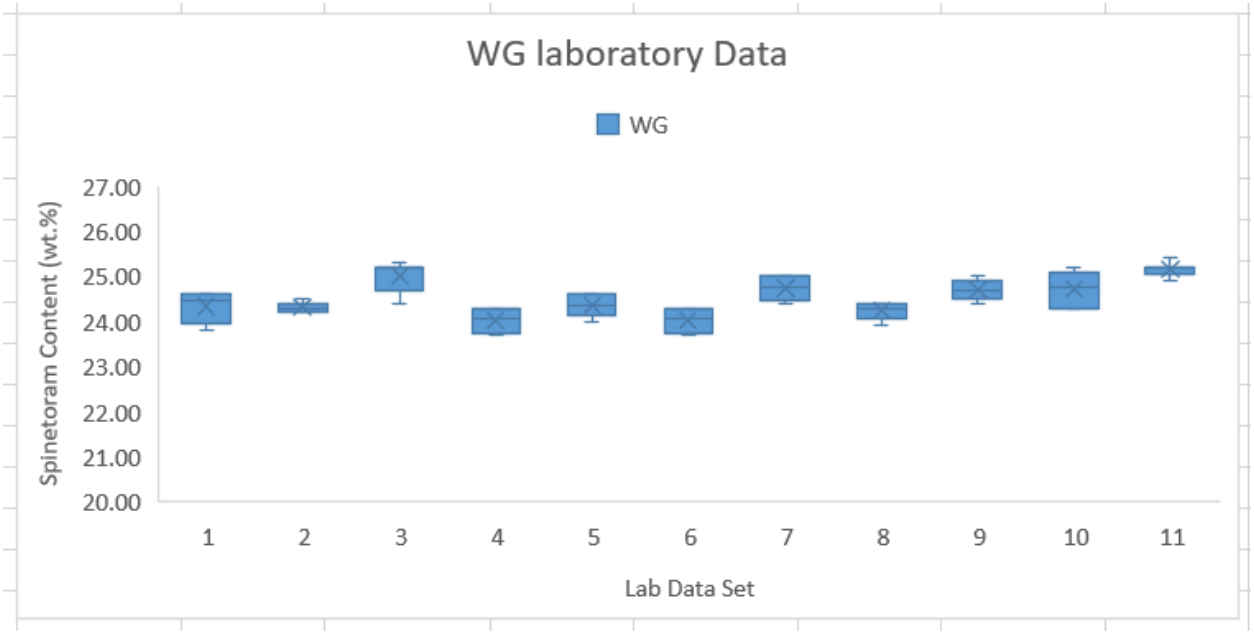
Appendix IV – SC1 Statistical Bar Chart



Appendix V – SC2 Statistical Bar Chart



Appendix VI – WG Statistical Bar Chart



Appendix VII – DT Statistical Bar Chart