4-(trifluoromethyl)-nicotinamide Collaborative study

Small scale collaborative study for the determination and differentiation of 4-(trifluoromethyl)-nicotinamide in TC by LC

Report to CIPAC

By

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1. Participants

Participating Laboratories are listed in alphabetical order in the table below. Laboratory numbers in the result tables were assigned, chronologically, based upon receipt of results.

Company / Lab	Contact	Country
BASF Limburgerhof	Simone Fuessl/Jürgen Fries	Germany
BASF Ludwigshafen	Rolf Förster	Germany
Bayer Frankfurt	Jörg Seltzer / Peter Wagener	Germany
Currenta GmbH, Dormagen	Michael Haustein	Germany
Syngenta Crop Protection AG	Christian Mink/Radek Bomba	Switzerland

2. General Information

4-(trifluoromethyl)-nicotinamide (TFMNA)

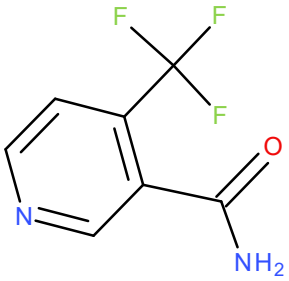
IUPAC name: 4-(trifluoromethyl)pyridine-3-carboxamide

Molecular mass: 190.1 g mol^{-1}

Empirical formula: C7 H5 F3 N2 O

CAS Number: 158062-71-6

Structure:



3. Samples

In total five samples of TC have been shipped together with reference standard to 5 participating labs, Syngenta conducted the trial twice.

- TFMNA TC– sample A
- TFMNA TC– sample B
- TFMNA TC– sample C
- TFMNA TC– sample D
- TFMNA TC– sample E
- TFMNA reference standard (purity 99.5 %w/w)

4. Method scope

The method is set up to determine the content of TFMNA by HPLC.

The sample is dissolved in acetonitrile and diluted with ACN/aq. 0.5% H3PO4 1/1. Quantification is done against external standard, by liquid chromatography using UV detection.

5. Procedure

Each sample was analyzed using four independent determinations: Two sample preparations double injected, analyzed on two different days.

6. Remarks

In table 1 the instruments, columns and chromatographic conditions noted by the participating laboratories are given.

Table 1: Chromatographic conditions used by the participants.

Lab	Instrument	Column
1	Agilent 1290 Infinity II	Kinetex Polar C18, 2.6 µm 150 mm 4.6 mm
2	Agilent 1200	Kinetex Polar C18, 2.6 µm 150 mm 4.6 mm
3	Agilent 1290 Infinity	C18 3 µm Polaris 150 x 4.6 mm Agilent
4	Agilent 1260 Infinity II	Kinetex Polar C18, 2.6 µm 150 mm 4.6 mm
5	Thermo Ultimate 3000	Kinetex Polar C18, 2.6 µm 150 mm 4.6 mm
6	Agilent 1260 Infinity II	Kinetex Polar C18, 2.6 µm 150 mm 4.6 mm
7	Agilent 1260 Infinity	Kinetex 2,6 µm Polar C18 100 A

No deviations to flow rate, detector wavelength or column temperature have been noted by the participants.

7. Evaluation and discussion

Data review

A data sets were included within the statistical assessment as no deviations were noted. In a second attempt only the laboratories using the conditions outlined in the method were considered and in a third approach a statistical straggler has been excluded.

Statistical results

In the tables 2 to 6 and the figures 1 to 5 the full set of analytical results of all participating laboratories is shown.

Table 2: Results of the different laboratories for Sample A.

	SAMPLE A		
	Day1	Day2	Mean
Laboratory 1	985.8	986.4	986.1
Laboratory 2	979.4	985.0	982.2
Laboratory 3	986.5	990.5	988.5
Laboratory 4	989.4	991.8	990.6
Laboratory 5	986.2	984.8	985.5
Laboratory 6	988.1	993.9	991.0
Laboratory 7	991.1	994.0	992.6

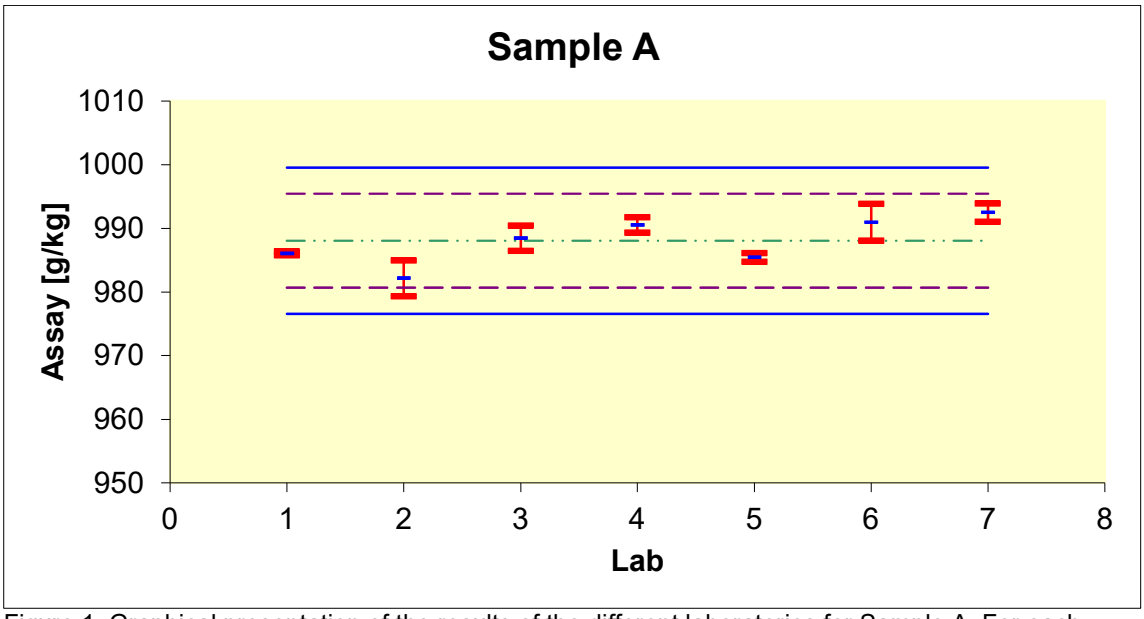


Figure 1: Graphical presentation of the results of the different laboratories for Sample A. For each laboratory (laboratories 1 to 7) the red bars represent day 1 and day 2, the blue bar represents the average.

Table 3: Results of the different laboratories for Sample B.

	SAMPLE B		
	Day1	Day2	Mean
Laboratory 1	992.7	992.9	992.8
Laboratory 2	986.8	993.7	990.3
Laboratory 3	995.9	997.6	996.8
Laboratory 4	995.8	998.5	997.2
Laboratory 5	990.2	1004.4	997.3
Laboratory 6	996.2	998.5	997.4
Laboratory 7	1001.0	999.0	1000.0

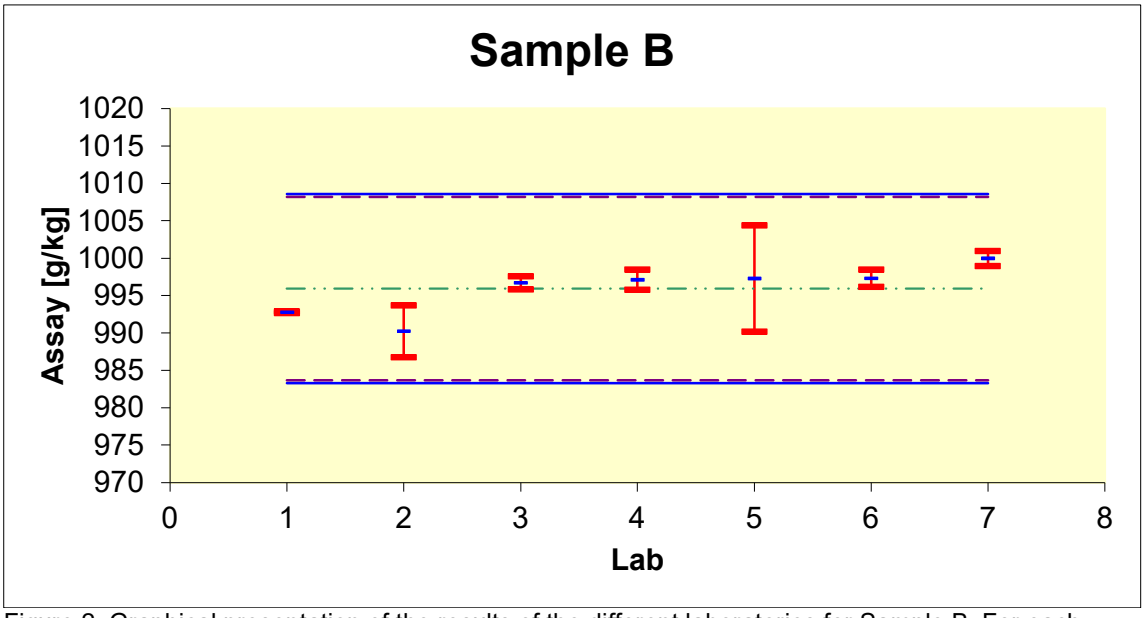


Figure 2: Graphical presentation of the results of the different laboratories for Sample B. For each laboratory (laboratories 1 to 7) the red bars represent day 1 and day 2, the blue bar represents the average.

Table 4: Results of the different laboratories for Sample C.

	SAMPLE C		
	Day1	Day2	Mean
Laboratory 1	991.6	992.6	992.1
Laboratory 2	988.2	993.6	990.9
Laboratory 3	1002.3	994.2	998.3
Laboratory 4	993.4	997.9	995.7
Laboratory 5	995.8	990.6	993.2
Laboratory 6	995.7	993.2	994.5
Laboratory 7	997.7	998.7	998.2

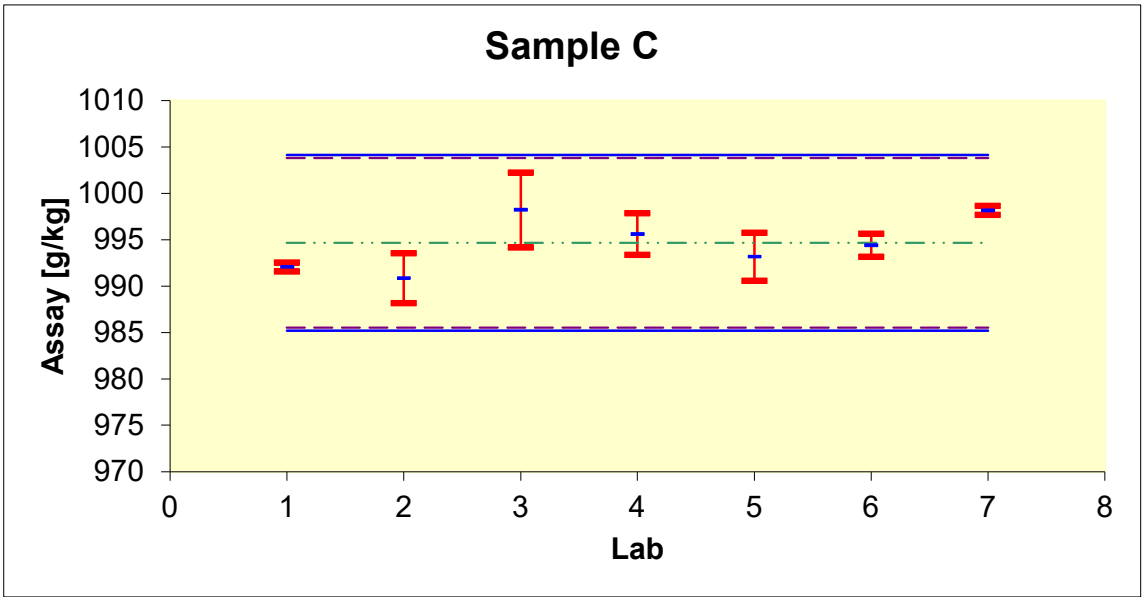


Figure 3: Graphical presentation of the results of the different laboratories for Sample C. For each laboratory (laboratories 1 to 7) the red bars represent day 1 and day 2, the blue bar represents the average.

Table 5: Results of the different laboratories for Sample D.

	SAMPLE D		
	Day1	Day2	Mean
Laboratory 1	996.1	990.8	993.5
Laboratory 2	989.4	1001.1	995.3
Laboratory 3	1000.0	996.4	998.2
Laboratory 4	995.7	999.7	997.7
Laboratory 5	994.4	990.9	992.7
Laboratory 6	995.8	1000.2	998.0
Laboratory 7	991.0	994.9	993.0

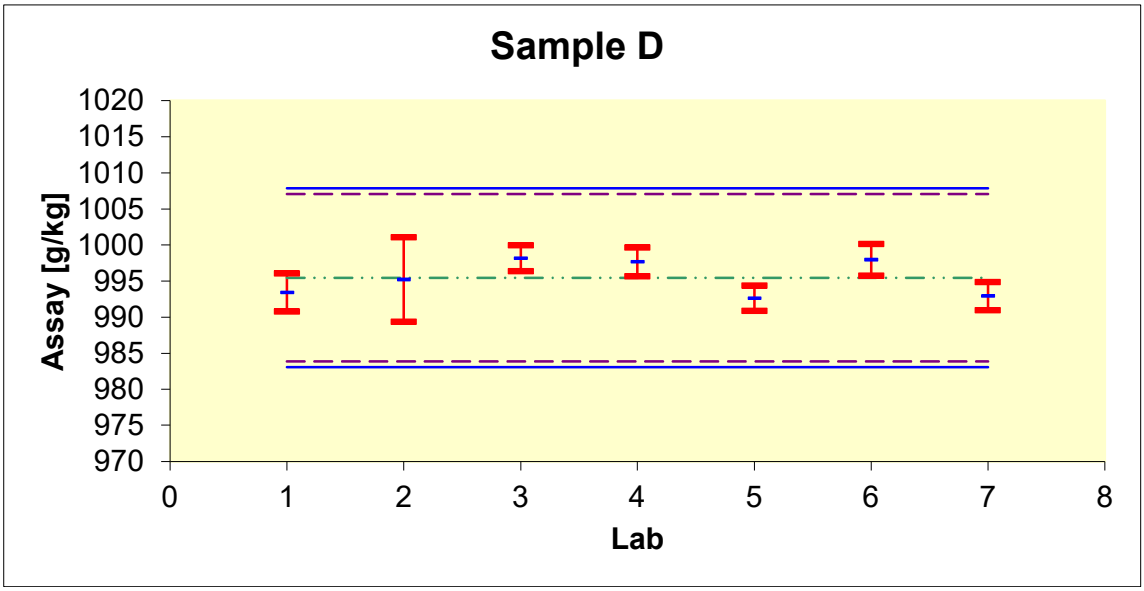


Figure 4: Graphical presentation of the results of the different laboratories for Sample D. For each laboratory (laboratories 1 to 7) the red bars represent day 1 and day 2, the blue bar represents the average.

Table 6: Results of the different laboratories for Sample E.

	SAMPLE E		
	Day1	Day2	Mean
Laboratory 1	993.8	991.5	992.7
Laboratory 2	992.3	998.5	995.4
Laboratory 3	1001.1	996.9	999.0
Laboratory 4	993.6	1000.8	997.2
Laboratory 5	994.6	1003.1	998.9
Laboratory 6	991.4	1000.3	995.9
Laboratory 7			

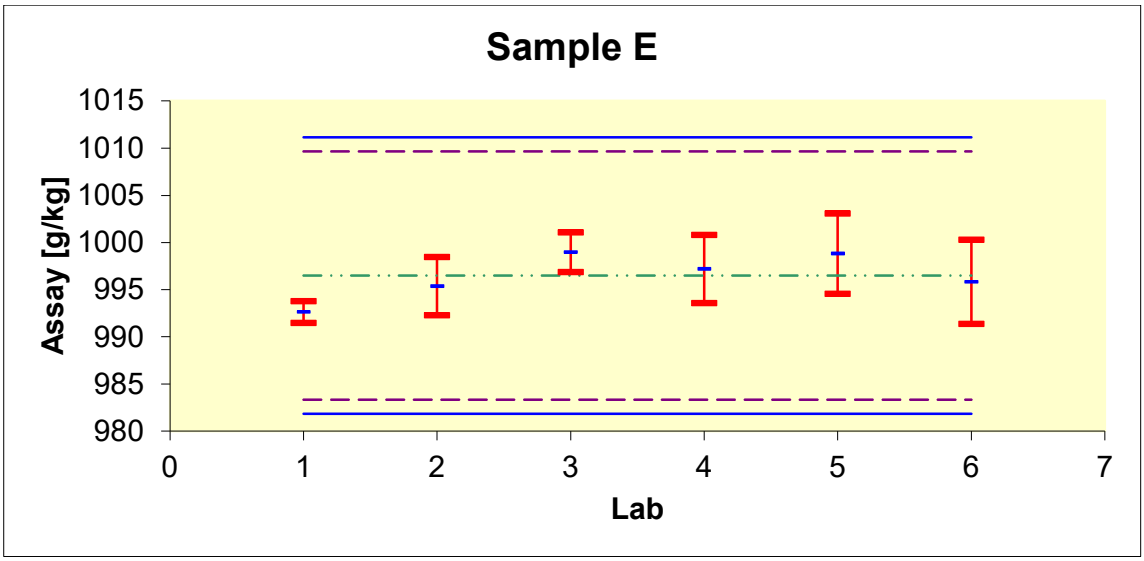


Figure 5: Graphical presentation of the results of the different laboratories for Sample E. For each laboratory (laboratories 1 to 7) the red bars represent day 1 and day 2, the blue bar represents the average.

Table 7: Overall statistics on all submitted results:

	SAMPLE A	SAMPLE B	SAMPLE C	SAMPLE D	SAMPLE E
Xm	988.1	995.9	994.7	995.5	996.5
L	7.0	7.0	7.0	7.0	6.0
Sr	2.6	4.4	3.3	4.1	4.7
SL	3.1	1.1	0.9	1.5	2.3
SR	4.1	4.5	3.4	4.4	5.2
r	7.4	12.3	9.1	11.6	13.1
R	11.5	12.6	9.5	12.4	14.6
RSDr	0.3	0.4	0.3	0.4	0.5
RSDR	0.4	0.5	0.3	0.4	0.5
RSDR(Hor)	2.0	2.0	2.0	2.0	2.0
Horrat	0.2	0.2	0.2	0.2	0.3

No Grubbs straggler or outlier have been identified. Even without elimination of any result the between laboratory experimental Relative Reproducibility Standard Deviation (RSDR) is below the acceptance limit based on the Horwitz curve calculation (RSDR(Hor)) for all samples.

8. Summary and Conclusion

A total of 7 laboratories participated in the trial, came back in time and provided results. For Sample E one sample was lost in transfer and only 6 results could be provided. The data sets from all these laboratories have been considered for the statistical evaluation (Figure 1 to 5 and Tables 2 to 7). In all cases shown in Tables 7 the Horrat is well below 1. No Grubbs straggler or outlier has been identified.

Syngenta considers this method to be suitable for the intended purpose and recommends going for a full collaborative trial for the determination of TFMNA in TC.