2015

SIEMENS

SIEMENS ULTRAMAT 6 IR CARBON MONOXIDE ANALYZER METHOD VALIDATION FOR TESTING CARBON MONOXIDE IN NITROGEN, NF

FINAL APPROVAL

This Methods Validation (MV) Summary Report, for the Siemens ULTRAMAT 6 IR Carbon Monoxide Analyzer, has been prepared by Integrated Project Services (IPS) and approved by IPS and Siemens.

Author — Mark Celii
Associated Director – Medical Gases, Compliance Services
Integrated Project Services
Date: 04Dec2015

Approver — Aaron Weinstein
Senior Director, Compliance Services
Integrated Project Services
Date: 08DEC2015

Approver — Dean Davis
Analytical Products and Solutions Quality Manager
Siemens USA
Date:

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1.0 OBJECTIVE

The objective of the analytical Method Validation (MV) protocol was to provide documented evidence that the Siemens ULTRAMAT 6 IR Carbon Monoxide Analyzer used to measure Carbon Monoxide in Nitrogen product is suitable for its intended purpose and is an equivalent, or better method for quantifying the Carbon Monoxide impurity levels, than the National Formulary compendial method for determining Carbon Monoxide in Nitrogen, NF.

The analyzer can be used to monitor bulk product in air separation plants, measure CO levels in Nitrogen after being filled in bulk liquid Nitrogen transports, and used for the analysis of filled cylinders.

The validation of the method demonstrates that it is suitable for its intended purpose.

2.0 SCOPE

This summary report provides the testing results and conclusions for the execution of the Siemens ULTRAMAT 6 IR Carbon Monoxide Analyzer method validation for the analysis of medical-grade Nitrogen in lieu of the NF compendial method.

3.0 DESCRIPTION AND BACKGROUND/DISCUSSION

3.1 Analyzer Description

The Siemens ULTRAMAT 6 IR Carbon Monoxide analyzer operates according to the infrared two- beam alternating light principle with double- layer detector and optical coupler.

The measuring principle is based on the molecule-specific absorption of bands of infrared radiation. The absorbed wavelengths are characteristic to the individual gases, but may partially overlap. This results in cross-sensitivities which are reduced to a minimum in the ULTRAMAT channel by the following measures:

- Gas- filled filter cell (beam divider)
- Double- layer detector with optical coupler
- Optical filters if necessary.

3.2 Measuring Principle

An IR source (5) which is heated to approx. 700 °C and can be shifted to balance the system, is divided by the beam divider (7) into two equal beams (sample and reference beams). The beam divider also acts as a filter cell.

The reference beam passes through a reference cell (11) filled with Nitrogen (a non-infrared-active gas) and reaches the right-hand side of the detector (12) practically unattenuated. The sample beam passes through the sample cell (10) through which the sample gas flows and reaches the left- hand side of the detector (13) attenuated to a lesser or greater extent depending on the concentration of the sample gas.

The detector is filled with a defined concentration of the gas component to be measured and is designed as a double- layer detector. The center of the absorption band is preferentially absorbed in the upper detector layer; the edges of the band are absorbed to approximately the same extent in the upper and lower layers. The upper and lower detector layers are connected together via the microflow sensor (15). This coupling means that the spectral sensitivity has a very narrow band.

The optical coupler (14) lengthens the lower detector chamber layer optically. The infrared absorption in the second detector layer is varied by changing the slider position (16). It is thus possible to individually minimize the influence of interfering components.

A chopper (8) rotates between the beam divider and the sample cell and interrupts the two beams alternately and periodically. If absorption takes place in the sample cell, a pulsating current is generated which is converted by the microflow sensor (15) into an electric signal.

The microflow sensor consists of two nickel grids heated to approx. 120 °C which, together with two further resistors, form a Wheatstone bridge. The pulsating flow together with the very close arrangement of the Nickel grids leads to a change in resistance. This leads to an offset in the bridge which is dependent on the concentration of the sample gas.

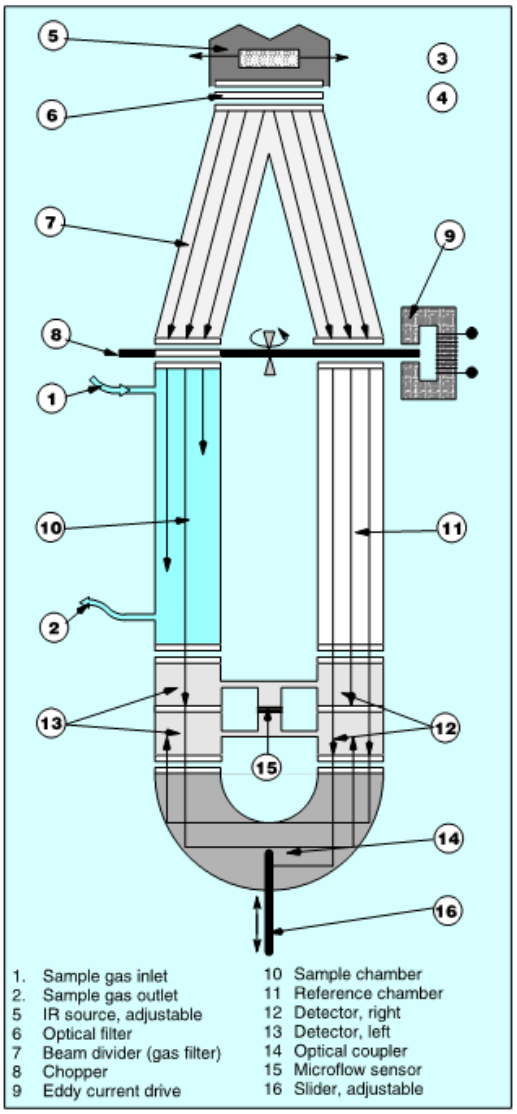


Figure 1 - Mode of Operation

4.0 METHODS VALIDATION SUMMARY

4.1 Test Gases

The following certified challenge gases were used to conduct the testing and represent the gas concentrations within the Dräger CO detector tube graduation scale, the limit of Carbon Monoxide in Nitrogen, NF, and include typical impurities in Nitrogen, NF.

- Challenge Gas #1…99.999% Nitrogen
- Challenge Gas #2…5.173 ppm Carbon Monoxide / Balance Nitrogen
- Challenge Gas #3…10.11 ppm Carbon Monoxide / Balance Nitrogen
- Challenge Gas #4…15.37 ppm Carbon Monoxide / Balance Nitrogen
- Challenge Gas #5…20.08 ppm Carbon Monoxide / Balance Nitrogen
- Challenge Gas #6…5.025 ppm Carbon Monoxide / 8.670 ppm Oxygen / Balance Nitrogen
- Challenge Gas #7…5.173 ppm Carbon Monoxide / 2.819 ppm Methane / Balance Nitrogen

4.2 Testing Conducted

The seven challenge gases were sampled using the Siemens ULTRAMAT 6 IR Carbon Monoxide analyzer as follows:

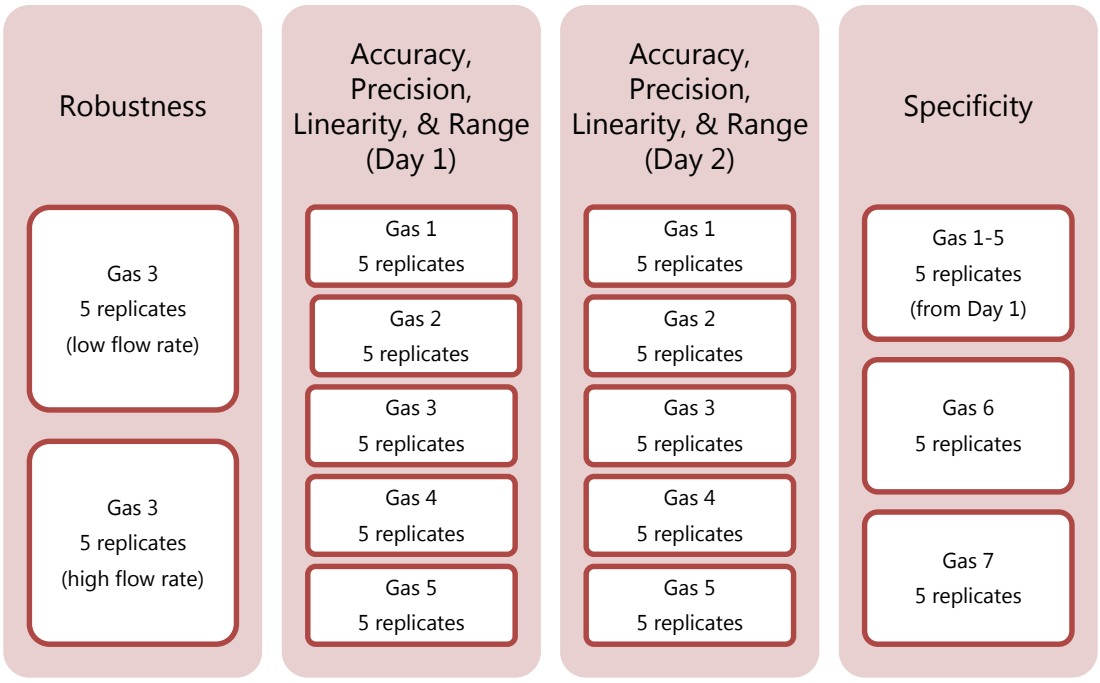


Figure 2 – IR Method Testing Conducted

The seven challenge gases were also sampled using a Dräger Carbon Monoxide detector tubes as follows:

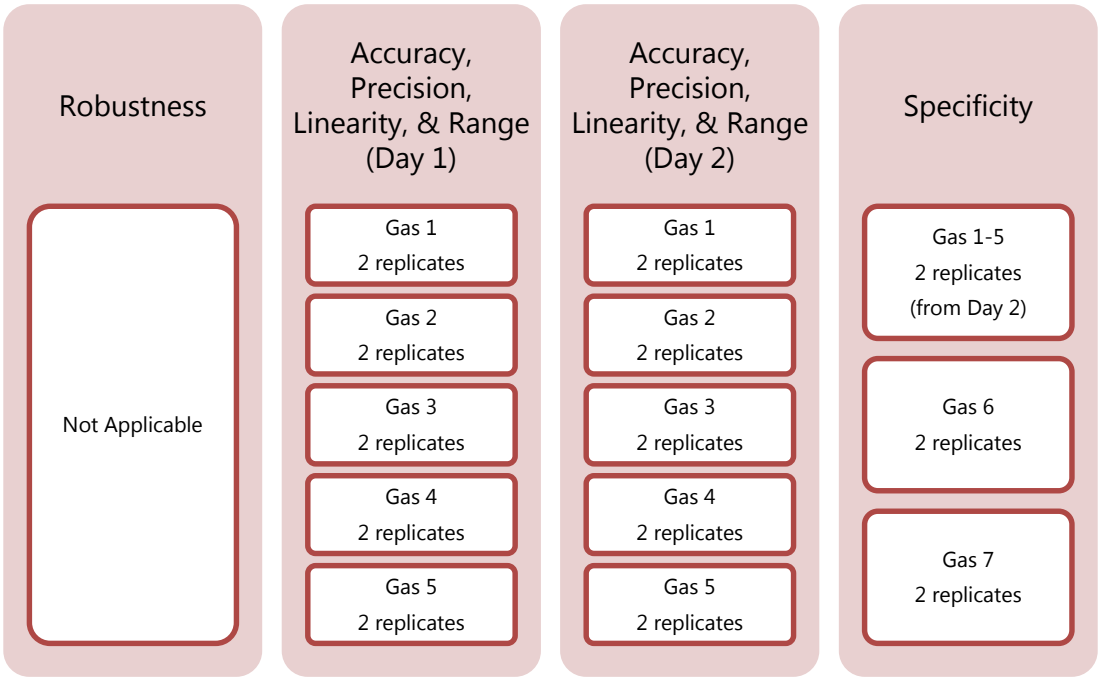


Figure 3 – Detector Tube Method Testing Conducted

4.3 Accuracy and Precision

Challenge Gases 1 through 5 were sampled on two separate days using both methods. Five (5) replicate samples were taken with the Siemens ULTRAMAT 6 IR Carbon Monoxide analyzer while two (2) replicate samples were taken with the Dräger detector tubes. The acceptance criteria used to evaluate accuracy and precision was:

- Accuracy: ± 1.0 ppm
- Precision: RSD (%) ≤ 2.0%

Table 1 below provides the result of the sampling conducted using the IR Method (all readings in ppm CO).

Table 1 IR Method Accuracy and Precision Results

Replicate #	Gas 1		Gas 2		Gas 3		Gas 4		Gas 5	
	Day1	Day2	Day1	Day2	Day1	Day2	Day1	Day2	Day1	Day2
1	0.00	0.00	5.12	5.08	10.13	10.11	15.32	15.24	20.33	20.10
2	0.00	0.00	5.14	5.09	10.15	10.12	15.31	15.23	20.31	20.12
3	0.00	0.00	5.14	5.11	10.12	10.12	15.32	15.16	20.25	20.17
4	0.00	0.00	5.14	5.10	10.16	10.09	15.29	15.20	20.32	20.19
5	0.00	0.00	5.14	5.10	10.12	10.12	15.31	15.20	20.30	20.18
Precision Calculations										
Average	0.000	0.00	5.136	5.096	10.136	10.112	15.310	15.206	20.302	20.152
Std Dev(σ)	0.000	0.00	0.009	0.011	0.018	0.013	0.012	0.031	0.031	0.040
RSD(σ_R)	n/a	n/a	0.174%	0.224%	0.179%	0.129%	0.080%	0.206%	0.153%	0.197%
Accuracy Calculations										
Conc. Of Std.	0.000		5.173		10.11		15.37		20.08	
Deviation From Std.[1]	0.000	0.000	0.037	0.077	0.026	0.002	0.060	0.164	0.222	0.072

Table 2 below provides the result of the sampling conducted using the Dräger detector tube method (all readings in ppm CO).

Table 2 Dräger Tube Method Accuracy and Precision Results

Replicate #	Gas 1		Gas 2		Gas 3		Gas 4		Gas 5	
	Day1	Day2	Day1	Day2	Day1	Day2	Day1	Day2	Day1	Day2
1	ND	ND	5	5	10	10	10-20	10-20	10-20	10-20
2	ND	ND	5	5	10	10	10-20	10-20	10-20	10-20
Precision Calculations										
Average	0.000	0.00	5	5	10	10	10-20	10-20	10-20	10-20
Accuracy Calculations										
Conc. Of Std.	0.000		5.173		10.11		15.37		20.08	
Deviation From Std.[1]	n/a	n/a	0.173	0.173	0.11	0.11	n/a	n/a	n/a	n/a

ND: Not Detected

[1] The absolute value of the deviation from standard is reported.

4.4 Robustness

Robustness testing was conducted on the Siemens ULTRAMAT 6 IR Carbon Monoxide analyzer only using five (5) replicate samples on Challenge Gas 3 at the minimum analyzer flow rate of 0.3 l/min (nominal) and at the maximum analyzer flow rate of 1.5 l/min (nominal). The acceptance criteria used to evaluate robustness was for the method to meet the accuracy and precision acceptance criteria at both the minimum and maximum flow rates tested. The results of the robustness testing are provided in Table 3 below.

Table 3 IR Method Robustness Results

Replicate #	Low Flow Rate	High Flow Rate
	0.3 lpm	1.5 lpm
1	10.09	10.08
2	10.11	10.10
3	10.09	10.09
4	10.10	10.09
5	10.07	10.10
Precision Calculations		
Average	10.092	10.092
Std Dev(σ)	0.015	0.008
RSD(σ_R)	0.147%	0.083%
Accuracy Calculations		
Conc. Of Std.	10.11	10.11
Deviation From Std. [2]	0.018	0.018

[2] The absolute value of the deviation from standard is reported.

4.5 Specificity

Challenge Gases 6 and 7 were sampled one time using both methods. Five (5) replicate samples were taken with the Siemens ULTRAMAT 6 IR Carbon Monoxide analyzer while two (2) replicate samples were taken with the Dräger detector tubes. The acceptance criteria used to evaluate specificity was for the results meeting the accuracy and precision acceptance criteria at each of the Carbon Monoxide concentrations. In addition, the qualitative results (Carbon Monoxide was detected or not) for the analyzer and the detector tube methods were required to be equivalent.

Table 4 IR Method Specificity Results

Replicate #	Gas 6		Gas 7	
	IR Method	DT Method	IR Method	DT Method
1	5.02	<5	5.00	5
2	5.04	<5	4.98	5
3	5.03		5.00	
4	5.02		4.99	
5	5.04		5.01	
Precision Calculations				
Average	5.030	<5	4.996	5
Std Dev(σ)	0.010		0.011	
RSD(σ_R)	0.199%		0.228%	
Accuracy Calculations				
Conc. Of Std.	5.025		5.004	
Deviation From Std. [3]	0.005	>0.025[4]	0.008	0.004
Qualitative Results				
Carbon Monoxide Detected	detected	detected	detected	detected

[3] The absolute value of the deviation from standard is reported.

[4] Calculated based on a certified standard of 5.025 ppm and the detector tube reading just below 5 ppm.

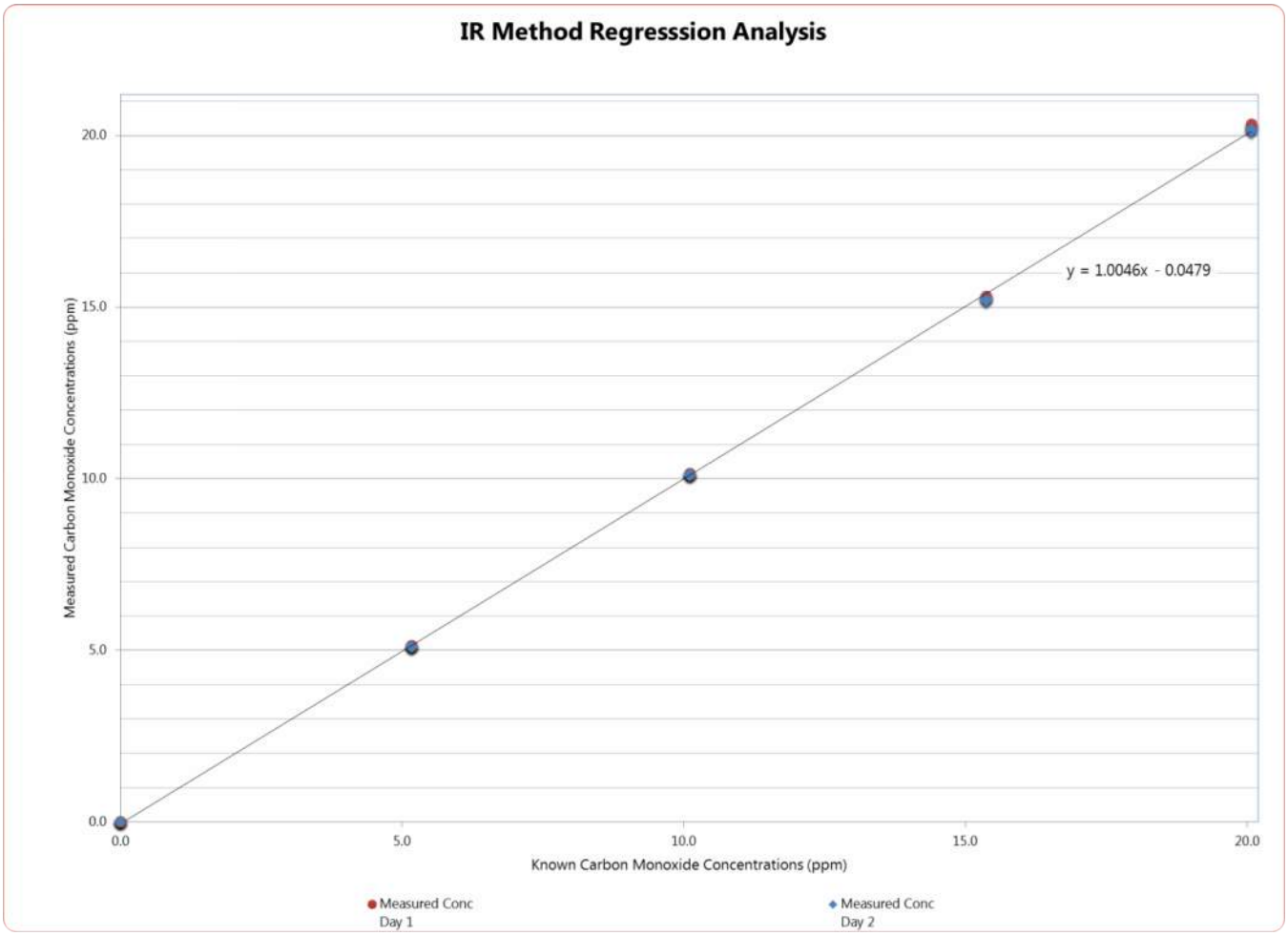
4.6 Linearity & Range

For the testing conducted in section 4.3, the measured Carbon Monoxide concentration as a function of the challenge gas Carbon Monoxide concentration for both the analyzer method and the detector tube method was plotted. A linear relationship was performed using the least squares method to determine the correlations of the two methods. The following acceptance criteria were used to evaluate the linearity of the methods:

- Correlation coefficient (r) ≥ 0.99
- y-intercept, slope of the regression line and the residual sum of squares will be reported

4.7 Linear Regression – IR Method

The linear regression for the IR method indicates a strong correlation between the measured and known Carbon Monoxide concentrations between 0 and 20 ppm Carbon Monoxide in Nitrogen.

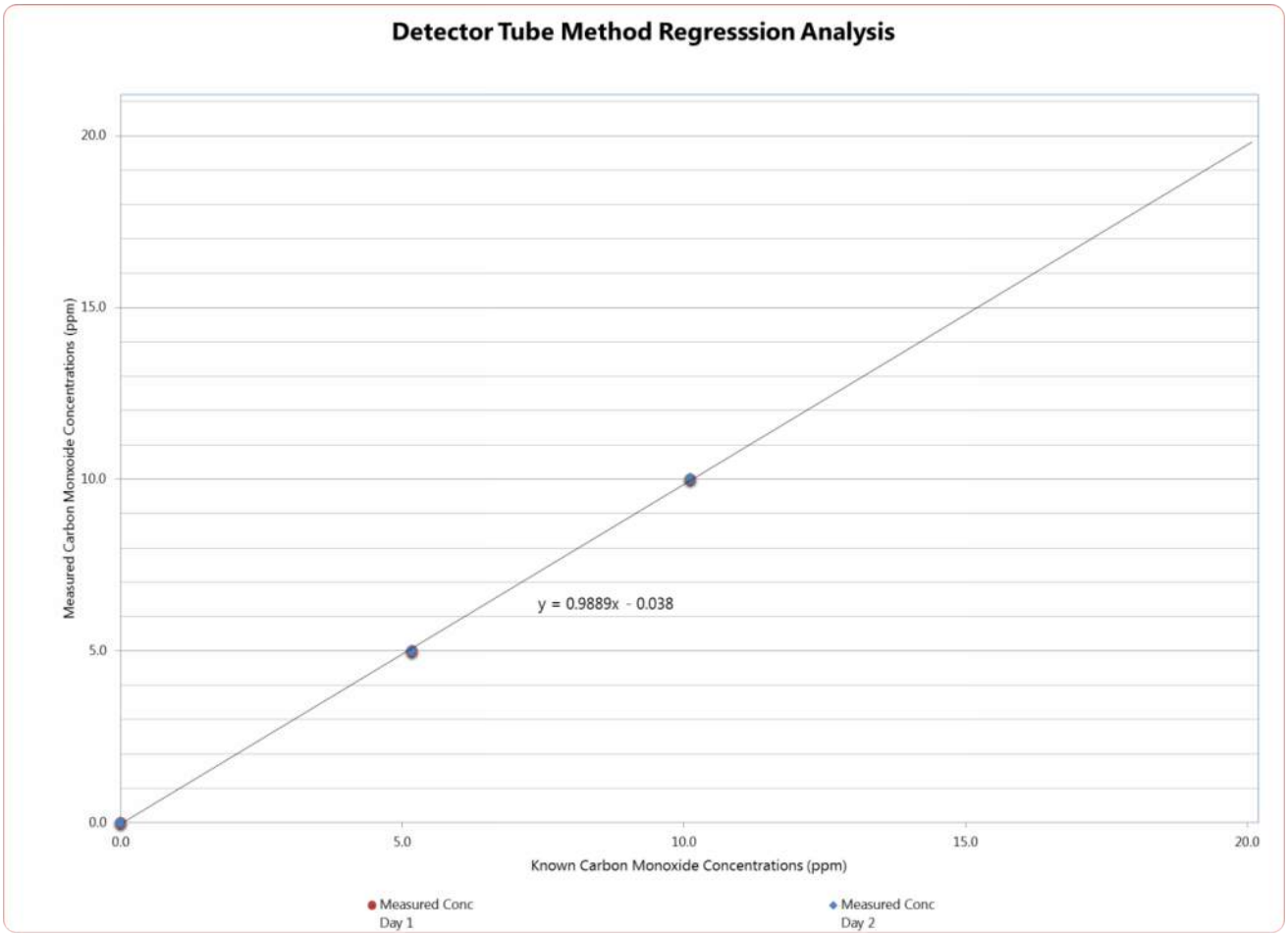


Challenge Gas No	Sample	Known Conc	Measured Conc Day 1	Measured Conc Day 2
1	Replicate 1	0.00	0.00	0.00
	Replicate 2	0.00	0.00	0.00
	Replicate 3	0.00	0.00	0.00
	Replicate 4	0.00	0.00	0.00
	Replicate 5	0.00	0.00	0.00
2	Replicate 1	5.173	5.12	5.08
	Replicate 2	5.173	5.14	5.09
	Replicate 3	5.173	5.14	5.11
	Replicate 4	5.173	5.14	5.10
	Replicate 5	5.173	5.14	5.10
3	Replicate 1	10.11	10.13	10.11
	Replicate 2	10.11	10.15	10.12
	Replicate 3	10.11	10.12	10.12
	Replicate 4	10.11	10.16	10.09
	Replicate 5	10.11	10.12	10.12
4	Replicate 1	15.37	15.32	15.24
	Replicate 2	15.37	15.31	15.23
	Replicate 3	15.37	15.32	15.16
	Replicate 4	15.37	15.29	15.20
	Replicate 5	15.37	15.31	15.20
5	Replicate 1	20.08	20.33	20.10
	Replicate 2	20.08	20.31	20.12
	Replicate 3	20.08	20.25	20.17
	Replicate 4	20.08	20.32	20.19
	Replicate 5	20.08	20.30	20.18

Parameter	Value	Acceptance Criteria
y-intercept:	-0.0479	reported
slope:	1.0046	reported
residual sum of squares:	0.42922	reported
correlation coefficient (r):	0.99992	≥ 0.99

4.8 Linear Regression – Detector Tube Method

When conducting the linear regression for the detector tube method, the regression was limited to the range of 0 to 10 ppm since the readings for Challenge Gas #4 and #5 were between 10 ppm and 30 ppm divisions on the detector tube and a specific value could not be obtained. The linear regressions indicate the IR method is exceeds the detector tube method within the subject range .



Challenge Gas No	Sample	Known Conc	Measured Conc Day 1	Measured Conc Day 2
1	Replicate 1	0.00	0	0
	Replicate 2	0.00	0	0
2	Replicate 1	5.173	5	5
	Replicate 2	5.173	5	5
3	Replicate 1	10.11	10	10
	Replicate 2	10.11	10	10
4	Replicate 1	15.37	10-20	10-20
	Replicate 2	15.37	10-20	10-20
5	Replicate 1	20.08	10-20	10-20
	Replicate 2	20.08	10-20	10-20

Parameter	Value[1]	Acceptance Criteria
y-intercept:	-0.0380	reported
slope:	0.9889	reported
residual sum of squares:	0.03632	reported
correlation coefficient (r):	0.99991	≥ 0.99

1. Linear Regression based on Challenge Gas 1-3 only.

5.0 DEVIATION SUMMARY

There were no deviations and no observations recorded during the execution of this protocol.

6.0 CONCLUSION

The Method Validation (MV) protocol for the Siemens ULTRAMAT 6 IR Carbon Monoxide Analyzer Method for Testing Carbon Monoxide in Nitrogen, NF has been successfully completed. There were no deviations or observations identified. Based on the results of the execution of the method validation protocol the Siemens ULTRAMAT 6 IR Carbon Monoxide Analyzer Method for Testing Carbon Monoxide in Nitrogen, NF Method has been demonstrated to be suitable for use and has been demonstrated to be at least equivalent to the NF method and therefore satisfies the requirement for equivalency.