



Evaluating Carryover when Using a QbD1200+ TOC Analyzer

Introduction

Cleaning is crucial in pharmaceutical manufacturing, and production process equipment must be thoroughly cleaned to ensure removal of Active Pharmaceutical Ingredients from the previous batch, as well as absence of contamination for the next batch. Total Organic Carbon (TOC) analyzers, such as the QbD1200+ TOC Analyzer, can be used during the cleaning validation process as well as for periodic cleaning verification.

Multiple samples can be analyzed on TOC analyzers to assess process cleanliness in multiple locations or to assess multiple manufacturing processes in a single run. Therefore, it's important to use a TOC analyzer that inhibits carryover from one sample to the next. Only then can users ensure accurate results and prevent false positives—suggesting that cleaning was ineffective even if it wasn't—potentially causing unnecessary delays and expenses. Carryover can also affect accuracy and reliability of cleaning validation data, potentially leading to non-compliance with regulatory requirements.

This technical note evaluates the ability of the QbD1200+ TOC analyzer to provide accurate results and virtually eliminate the potential for carryover.

Objective

The goal is to assess the ability of the QbD1200+ analyzer to deliver accurate results for low TOC concentration, even when a high TOC sample was analyzed immediately prior. It will be achieved by evaluating carryover when analyzing blank samples after standard samples of increasing TOC concentrations with standard measurement parameters. For consistency between measurements, tests have been performed using the autosampler.

Procedure

1. Set up the QbD1200+ analyzer for four replicate runs, do not reject the first replicate, and report data as PDF and csv files for record keeping. Set the measurement parameters as per Figure 1.
2. Prepare blank and concentration standards at 500 ppb, 1,000 ppb and 10,000 ppb of carbon.
3. Analyze samples in this sequence:
 - Blank x3
 - 500 ppb
 - Blank
 - 1,000 ppb
 - Blank
 - 10,000 ppb
 - Blank

Note: Because the analyzer's Autorange mode is **off** for this experiment, measurement of the 10,000 ppb standard is not expected to be accurate.

Figure 1: QbD1200+ TOC Analyzer measurement parameters to evaluate carryover.

Results are shown in **Table 1**. The average water blank value was calculated on 3 measurements. Average Water Blank Adjusted Concentration was calculated as the difference between the measured concentration of blank samples and the average water blank concentration.

Date	Sample Concentration (ppb)	Measured Concentration (ppb)	Average Water Blank Adjusted Concentration (ppb)
9/17/2024	Water Blank	6	
9/17/2024	Water Blank	5.3	
9/17/2024	Water Blank	4.9	
	Average Water Blank	5.4	
9/17/2024	500 ppb	501	
9/17/2024	Water Blank	5.6	0.2
9/17/2024	1,000 ppb	987	
9/17/2024	Water Blank	5.4	0
9/17/2024	10,000 ppb	9275	
9/17/2024	Water Blank	6.8	1.4

Table 1: Values correspond to the average of four replicate runs for each sample. The Average Water Blank is the average value of 3 consecutive measurements with four replicate runs of the Water Blank.

These results demonstrate that the QbD1200+ TOC Analyzer is not sensitive to carryover. The instrument showed no significant carryover after analysis of 500 ppb and 1,000 ppb. After the measurement of a 10,000 ppb sample, the system shows 0.01% of carryover ($1.4 / 10,000 * 100 = 0.014\%$), which remains at the level of the standard deviation for such low-level concentrations.

Conclusion

The results from this experiment demonstrate that the QbD1200+ TOC Analyzer virtually eliminates potential carryover. It can provide accurate results for low concentrations of TOC, even with wide variation in concentrations between samples, thereby maximizing uptime by avoiding false positives.

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