TOC System Suitability Test – Redefined According to New USP Regulations

Challenge

After revision of USP TOC monographs, a wider concentration range has to be covered by the TOC method applied and an SST test at 8 ppm must be passed.

Solution

Adapted calibration strategy to cover a TOC working range up to 20 ppm and successful application of the state-of-the art SST test sequence in the multiWin software.

Introduction

The USP <643> represents the general method for TOC testing in pharmaceutical applications and provides guidance on how to qualify the analytical technique for use as well as guidance on how to interpret instrument results for use as a limit test.

The revised TOC monograph <643> was implemented with the release of USP 37. It now describes two different TOC testing approaches addressing different pure water qualities, which are "Bulk Water" (e.g., Purified Water [PF], Water for Injection [WFI], Water for Hemodialysis, and condensate of Pure Steam) and "Sterile Water" (e.g., Sterile Water for Injection [SWFI], Sterile Purified Water [SPW], Sterile Water for Irrigation, and Sterile Water for Inhalation).

For bulk water quality, the testing procedure and limit values were retained as established:

Parameter	Values
Detection limit for the applied TOC analyzer	0.05 mg/L (ppm)
TOC limit for sample testing	0.5 mg/L
SST concentration level	0.5 mg/L
Max. preparation water TOC blank	0.1 mg/L

For the sterile water quality, the testing procedure was slightly modified and new limit values were established as follows:

Parameter	Values
Detection limit for the applied TOC analyzer	0.1 mg/L (ppm)
TOC limit for sample testing	8.0 mg/L
SST concentration level	8.0 mg/L
Max. preparation water TOC blank	0.5 mg/L

This application note demonstrates that the multi NC pharma allows straightforward and reliable TOC testing for sterile water according to the newly established SST.

Materials and Methods

Sample Preparation and Measurement

Samples were taken from tap water and water from a filtration plant, where different filters were applied to clean up raw water. The samples had been stored in the refrigerator at 4 °C. System suitability test solutions of 8 mg/L sucrose and p-benzoquinone, respectively, were prepared from 100 mg/L stock solutions by dilution with ultrapure water from the ultrapure water plant in the lab and subsequently run with the SST sequence integrated in the software before the samples were measured.

After several rinse steps the samples were filled into 40 mL sampler vials, sealed with aluminum foil, and placed into the AS vario sample rack. Using the autosampler, the samples were acidified with 1 M H_2SO_4 (multi N/C pharma UV) and 2 M HCl (multi N/C 3100 pharma), respectively, and subsequently purged with the carrier gas according to the method settings for complete TIC removal prior to NPOC measurement.

During the oxidation process in the high-power, long-life UV reactor or in the Pt catalyst filled combustion tube, respectively all carbon compounds are quantitatively converted to CO_2. The wide-range Focus Radiation NDIR Detector was used for quantitative determination of CO_2 content in the measurement gas.

Calibration

The multi N/C pharma analyzers were calibrated for NPOC in the range from 0.2 to 20 mg/L with standard solutions prepared from a 1000 mg/L sucrose stock solution. A multipoint calibration type was used. The calibration curve and its characteristics are shown in Figure 1.

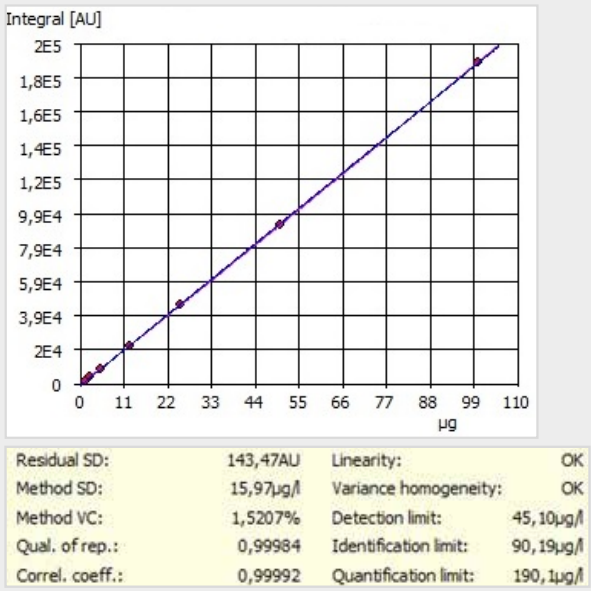

Figure 1: NPOC calibration curve and characteristics

Instrumentation

The following method settings were used to determine the TOC content:

Table 1: Method settings

Parameter	multi N/C pharma UV	multi N/C pharma HT, multi N/C 3100 pharma
Measurement parameters	NPOC	NPOC
Digestion	UV radiation assisted by $Na_2S_2O_8$	high temperature oxidation using Pt catalyst at 800 °C
Number of single repetitions	min. 3, max. 4	min. 3, max. 4
NPOC purge time	360 sec	360 sec
Rinse with sample before injection	3 times	3 times
Injektion volume	5 mL	2 mL (multi N/C pharma HT), 1 mL (multi N/C 3100 pharma)

Results and Discussion

After system calibration, 2 tap water and 2 filtrated water samples were measured as described above and subsequent SST sequence run. Results are displayed in the table below.

Table 2: Results

Sample ID	NPOC Average [mg/L]	NPOC RSD [%]
Tab Water 1	0.856	1.1
Tab Water 2	1.231	0.8
Filter 1	4.638	0.5
Filter 2	9.893	0.7

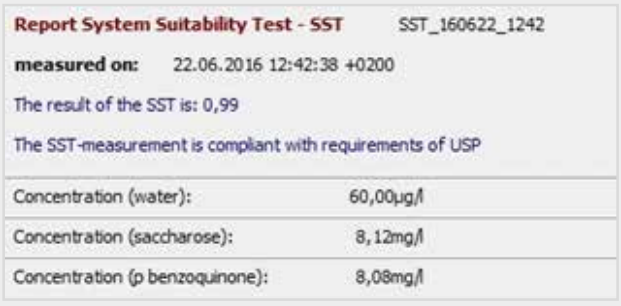

Figure 2: multiWin SST report

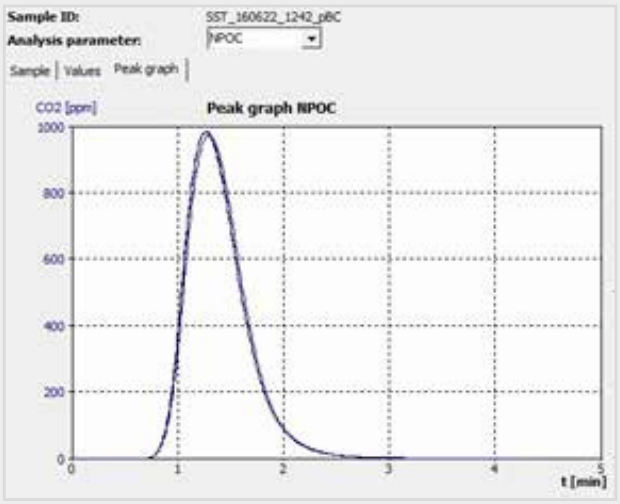

Figure 3: TOC peak graph for p-benzoquinone SST solution

Conclusion

The revision of the TOC-related USP monograph has broadened the pharma application range for TOC analyzers. Additionally, a new monograph USP <661.1> was implemented for testing of extractables from packing materials. According to this method, purified water extractions from polymer packing materials are prepared under the described conditions and tested for TOC within 4 hours after preparation according to USP <643>. The TOC method to be used needs to provide a linear dynamic range from 0.2 to 20 mg/L TOC with a detection limit of max. 0.2 mg/L.
This application note clearly demonstrates that the multi N/C pharma analyzers with their high-oxidation power and sophisticated design provide the required performance characteristics for the new challenges in pharmaceutical TOC testing beyond the 500 ppb limit.

References

Bletzinger, B.; Êtes-vous prêt à relever les exigences du TOC des nouvelles méthodes USP? La Gazette, September 2016
Bletzinger, B.; Are you fit for the TOC challenges according to new USP regulations? GIT Labor-Fachzeitschrift, October 2016

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