

Application News

No. SCA-130-206

Sum parameter – Total Organic Carbon

TOC – Determination according to USP 643 (USP 36-NF 31)

In 1996, the US Pharmacopeia has introduced the TOC parameter for the determination of impurities in purified water and water for injections. For other waters used in the pharmaceutical industry, the wet-chemical potassium permanganate test continued to be used. Meanwhile however, TOC determination has proven to be so effective that it now replaces the wet-chemical test.



In the current version of the UPS <643> (USP 36-NF 31) a distinction is made between 'bulk water' and 'sterile water'. The chapter 'Bulk Water' includes purified waters that are to be used right away as purified water, water for injection, water for hemodialysis and as condensate of pure steam. The following known conditions apply to TOC determinations:

Limit of detection:	< 0.05 mg/L C
Blank water, r_w :	max. 0.1 mg/L C
Standard (sucrose), r_s :	0.5 mg/L C
SST (benzoquinone), r_{ss} :	0.5 mg/L C
Permitted response:	85 – 115%
Limit response (waters) r_u :	< ($r_s - r_w$)

The chapter 'Sterile Water' is new. It includes sterile purified water, sterile water for injections, sterile water for irrigation and sterile water for inhalation. Sterile water can be stored in various packaging configurations. In comparison to bulk water, however, other conditions for TOC determination apply:

Limit of detection:	< 0.05 mg/L C
Blank water, r_w :	max. 0.1 mg/L C
Standard (sucrose), r_s :	8 mg/L C
SST (benzoquinone), r_{ss} :	8 mg/L C
Permitted response:	85 – 115%
Limit response (waters) r_u :	< ($r_s - r_w$)

■ Impact of the new determination

The present requirements of the UPS <643> (bulk water) are consistent with the requirements of the European Pharmacopeia (limit of detection, concentration of the standard solution (sucrose) and system suitability solution (benzoquinone and response). Validation of the TOC system for both determinations is therefore sufficient.

In accordance with the new USP <643>, the implementation of a system suitability test using higher concentrations is required.

For users of Shimadzu's TOC systems, this just means the creation of an additional calibration curve (sucrose, 8 mg/L, see figure 1) and control sample (benzoquinone, 8 mg/L, see figure 2) as well as extension of the current validation process with these data.

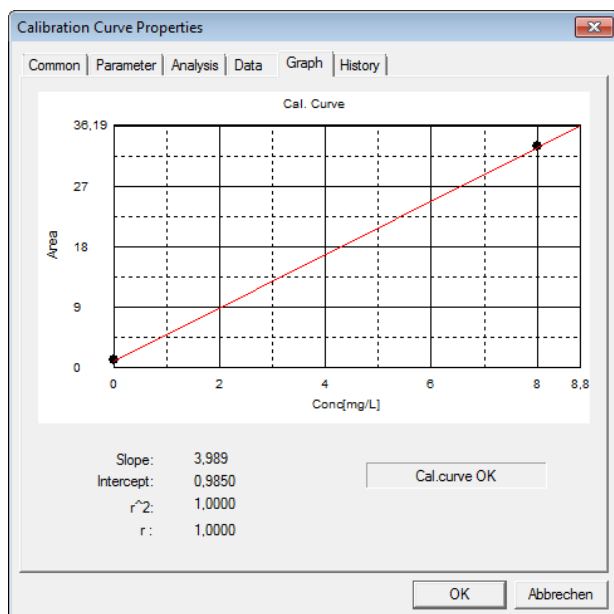


Figure 1 : Calibration Curve, Sucrose 8mg/L

Additional modifications of the TOC system are not necessary.

■ Shimadzu TOC-System

Shimadzu offers two systems that are ideally suitable for TOC determination in ultrapure water. The TOC-VWP/WS uses wet-chemical oxidation, whereas the TOC-LCPH uses catalytic combustion at 680 °C. With their wide measuring range of 0.5 µg/L up to 30,000 mg/L, the instruments support any application – from ultrapure water (for

instance in cleaning validation) to highly polluted waters (such as wastewaters). Shimadzu TOC-Systems.

Both types of instrument with their different oxidation methods can be used for TOC determination in accordance with the new United States Pharmacopeia (USP <643>) and the European Pharmacopeia (EP 2.2.44). The advantage of the combustion method is its high oxidation potential, especially for samples containing particulate matter. Moreover, simultaneous TOC/TN_b measurements can be carried out, leading to a higher information content of the analysis. The advantage of wet-chemical oxidation is its very high injection volume, which leads to higher sensitivity and therefore enables high precision measurements in the lower ppb range.

■ Recommended Analyser / Configuration

TOC-L_{CPH} with high sensitive catalyst
ASI-L (40ml), external sparge kit

TOC-V_{WP}

ASI-V (40ml), external sparge kit

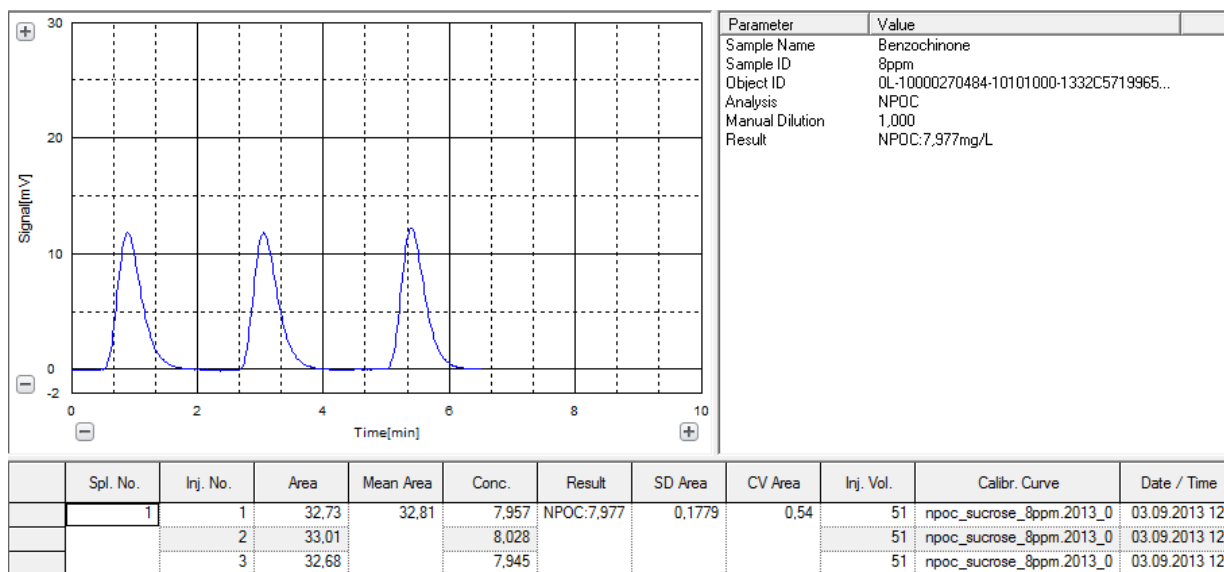


Figure 2: SST, Benzochinone 8mg/L