

Application News

No. SCA-130-203

Sum parameter – Total Organic Carbon

TOC –Determination in cleaning validation - swab method

Cleaning validation substantiates the effectiveness of a cleaning process and ensures that no residues remain on the surfaces of the production equipment. For the detection of contaminations, validated analytical methods must be used that are sensitive enough to determine the defined acceptable residue level. In general, residue limits of 10 ppm or 1/1000 of the usual therapeutic dose of an active substance are used as acceptance criteria.



■ Cleaning methods: Clean out of Place

For COP cleaning, the entire production system must be disassembled and the components must be cleaned individually. This procedure is very time consuming and labor intensive. Due to the individual cleaning, this procedure cannot be standardized. Advantages are, however, the low investment costs of the system and the possibility of visual inspection.

■ Sampling and analysis

In COP cleaning, the wiping method (swab) is used for sampling of visible residues. These include coatings, crusts, material deposited in corners and edges, and especially poorly soluble substances. The swab can be extracted in a solvent and the extracted solution is subsequently analyzed. If water is used for extraction, TOC analysis is suitable for subsequent analysis. Alternatively, the swab can also be measured directly (using a carbon-free swab) using a TOC solid-sample module.

■ Measuring system for the swab test

The modular design of Shimadzu's TOC-L series now enables the additional determination of the swabs using the same instrument. For this purpose, a solid-sample module (SSM-5000A) was connected to the main instrument, either a TOC-L series combustion system or the wet-chemical model of the TOC-V series.



For TC determination, the swab is placed in a ceramic boat and transferred into the oven, which is heated to 900 °C.

There, all carbon compounds are oxidized to CO₂. To ensure complete oxidation, there is an additional catalyst in the combustion tube. The resulting CO₂ is then transported to the detector in the main instrument. The NDIR detector of the TOC-L series contains a tandem cell that consists of a long cell (200 mm) and a short cell (1 mm). By default, the long cell is used for water analysis and the short cell for solid-sample analysis. To attain a higher sensitivity for the analysis of solids, the solid-sample module can also be connected to the long, and thus the more sensitive, measuring cell. This can be realized using an upstream switching valve. This way, the system can now readily be used for cleaning validation without any loss in flexibility of switching between water and solid-sample analysis.

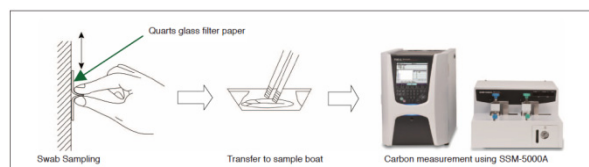
■ Preparation

As the TOC analysis involves a sum parameter, it is important to ensure that the measured carbon really originates from the sampled surface. Some preparation is, therefore, important.

First, the swabs used must be carbon-free. This is why fiber optics swabs are used, which are annealed at 600 °C and are stored under dry conditions using an inert gas. The same pretreatment is required for the ceramic boat. All tools used, such as tweezers and glass containers must be free from carbon.

■ Swab test

For the wiping test, two pretreated swabs are sampled, the lower swab is moistened with water and the defined surface is wiped according to the prescribed procedure. The used swab is now folded, placed in the clean ceramic boat and transferred to the TOC measuring system.



Depending on the expected concentration or defined limit value, the system configuration and calibration curve is selected. The calculated amount of carbon is now correlates directly to the area of the wiped surface.

■ Practical example:

■ Instrument/ Measurement parameter

Unit: TOC-LCPH + SSM-5000A
(shortcut of IC-flow line)

Detector cell: Short Cell

Carrier gas: 400 mL/min oxygen (SSM)

Meas.-typ: TC

Cal-Curve: 1-Point Calibration curve with 30µL of 1%C Glucose solution

Swab: Advantec QR-100 quartz glass Filter paper (45 mm)
Prepared at 600°C, 15min

■ Result

Compound	TOC-Result	Recovery
Blank	0,00	
Tranexamic acid	202 µgC	101 %
Anhydrous caffeine	201 µgC	100 %
Isopropylantipyrine	210 µgC	105 %
Nifedipine	212 µgC	106 %
Gentashin ointment	200 µgC	100 %
Rinderon ointment	209 µgC	104 %

(Further information is available in the application note Japan TOC O41)