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Application News

No. SCA-130-208

Sum parameter – Total Organic Carbon

TOC – Determination according to USP 661.2 Testing of Plastic Packaging Systems and their Materials of Construction

In the pharmaceutical industry plastic packaging is used in various forms – for example for intravenous bags, bottles, cartridges or pre-filled syringes. The packaging must be tested for suitability for these uses. It is published in USP 39-NF34, which will be valid from May 2016.

Besides to the change of the title “Plastic Packaging Systems and their materials of Construction”, two new chapters are established.

This application note is related to the second chapter 661.2.

■ 661.2 Plastic packaging system

This chapter deals with the required testing of the final packaging system since packaging often consists of than one plastic material. Characterization takes place by identifying and determining the biocompatibility, general physicochemical properties and Additives.

The TOC Parameter as an indicator for extractable organic material is part of the physio-chemical characteristics that must be determined.

For testing the packaging system, it is filled with ultra-pure water, sealed and heated in an autoclave. The temperature and dwell time depend in the plastic used. In order to determine the blank value, ultra-pure water is poured into a glass flask and heated to the same temperature. The TOC of both solutions is determined. The difference between the two measured TOC values should not exceed 8mg/L.

■ TOC determination in pharmaceutical application

The TOC determination is performed according to the USP<643>. This regulation describes the TOC determination for pure water, purified water and water for injection. It does not prescribe any particular oxidation technique for TOC determination.

The TOC systems, however, must be able to differentiate between inorganic and organic carbon. This can be carried out either via removal of the inorganic carbon (NPOC method), or via a separate determination (difference method). The limit of detection for TOC should be at least 0.05 mg /L. The applicability of the method must be determined via a system suitability test.

However, material extracts may have TOC values that are higher than those of purified water because of extracted organic substances.

Thus the TOC analyses performed should have a limit of detection of 0,2mg/L and should have a demonstrated linear dynamic range from 0,2 – 20mg/L.

■ 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.
Both types of instrument with their different oxidation methods can be used for TOC determination in accordance with the United States Pharmacopeia (USP <643>) and the European Pharmacopeia (EP 2.2.44).

■ Linear dynamic range from 0,2 – 20mg/L

To prove the required dynamic range, a calibration with TOC-L CPH (with high sensitivity catalyst) was carried out in a range of 1,0 mg/L – 20mg/L.

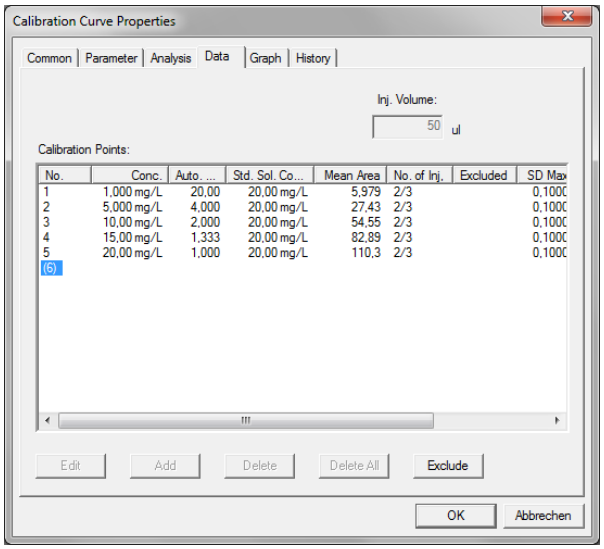

Figure.1 : Calibration Curve 20mg/L, results

For the dilutions, the automatic dilution function of the TOC-L system was applied. The injection volume is determined, based on the highest calibration standard. For 20mg/L the default injection volume is 50µl.

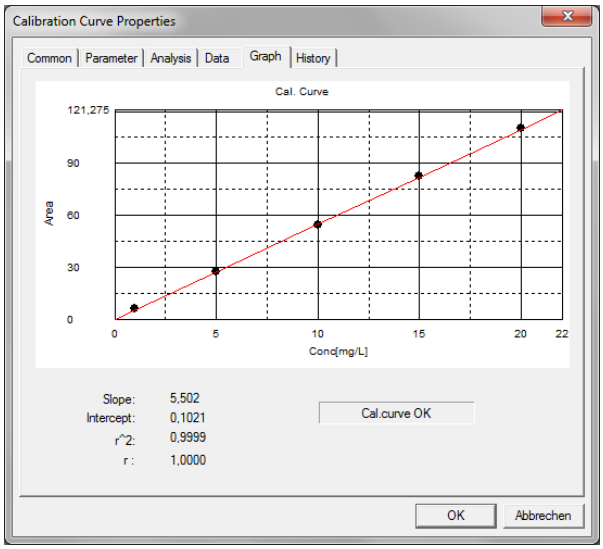

Figure.2 : Calibration Curve 20mg/L, graphic

The calculation of the limit of detection limit according to DIN 32645:

Characteristics

Slope a:	5,503
Intercept b:	0,091
Correlation coefficient r:	0,9999
Result uncertainty:	33,3%
Probability of error (a):	5,00%
Number of injections:	2

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Limit of detection: 0,2mg/L

These results show that the TOC-CPH with high sensitivity catalyst covers the required linear dynamic range from 0,2 – 20mg/L. This means both applications, purified water and this extraction solution can be measured with a single TOC-L CPH instrument.

■ Recommended Analyzer / Configuration

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

■ **Source**: www.usp.org

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