

Standard Operating Procedure

Title: Calibration for the TOC Analyzers

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1.0 Purpose

The objective of this procedure is to provide instructions on how to calibrate the Total Organic Carbon Analyzer.

2.0 Scope

This procedure applies to the calibration, blanking, and the calibration verification operations of the Total Organic Carbon Analyzers. The focus of this procedure is the TOC Mode of operation in Range 2 of the analyzer. The calibration procedure can also be applied to all other modes and ranges by changing the concentration of the standards to match the range and mode that are being independently calibrated.

3.0 Authority and Responsibility

- 3.1 The Director of Process Analytics/Quality Control (PA/QC) has the authority to define this procedure.
- 3.2 PA/QC is responsible for training laboratory personnel and documenting this training to Biopharmaceutical Quality Assurance (BQA).
- 3.3 PA/QC personnel are responsible for the performance of this procedure.
- 3.4 PA/QC is responsible for reviewing the data and documentation of the results of this procedure.
- 3.5 Biopharmaceutical Quality Assurance (BQA) is responsible for quality oversight of this operation.

4.0 Materials and Reagents

- 4.1 Sodium Persulfate $\text{Na}_2\text{S}_2\text{O}_8$ BDP Part Number: 30134
 - 4.1.1 Grade: Reagent Grade 98% or higher
 - 4.1.2 Use: 10% in reagent
- 4.2 Phosphoric Acid H_3PO_4 BDP Part Number: 30536
 - 4.2.1 Grade: NF Reagent Grade 85%
 - 4.2.2 Use: 5% (by weight) in persulfate reagent and 21% (by weight) in acid reagent
- 4.3 1, 4 – Benzoquinone $\text{C}_6\text{H}_4\text{O}_2$ BDP PN: 30005
 - 4.3.1 Grade: USP reference Standard <11> or equivalent

See **SOP 22919 - Standard Preparation for TOC Analyzer.**
- 4.4 Sucrose BDP PN: 30340
- 4.5 Reagent Water (H_2O)

The reagent water used must be of the highest quality deionized, distilled or reverse osmosis water available, containing no more than 0.1 ppmC for low-level analysis. See **SOP 22917 - Operation of the Phoenix 8000 TOC Analyzer**, for the recommended source that provides water of this quality.
- 4.6 Sampling Containers BDP PN: 20442

All TOC tubes coming into contact with the calibration standards must be clean.

5.0 Calibration Procedure – Performed Weekly

5.1 Shimadzu TOC Analyzer

5.1.1 Set-up Analyzer

- 5.1.1.1 Verify that the Shimadzu TOC Analyzer is turned on and ready to operate by performing the daily maintenance checks in Section 5.1 of **SOP 22922 - Preventative Maintenance for the TOC Analyzers.**

5.1.1.2 Prepare calibration standards to be analyzed using Standard Operating Procedures **SOP 22919 - Standard Preparation for TOC Analyzers** and **SOP 22918 - Glassware Cleaning for Trace TOC Analysis**.

5.1.1.2.1 The recommended and used concentration of the calibration standards for **TOC Range 0.01 – 20 ppm C** are:

5.1.1.2.2 “0” ppm C Blank Water

5.1.1.2.3 0.2 ppm C SUCROSE/H₂O

5.1.1.2.4 0.5 ppm C SUCROSE/ H₂O

5.1.1.2.5 1.0 ppm C SUCROSE/ H₂O

5.1.1.2.6 2.0 ppm C SUCROSE/ H₂O

5.1.1.2.7 5.0 ppm C SUCROSE/ H₂O

NOTE: 1,4 Benzoquinone, Sucrose, or KHP (all in water) can be used to make up the calibration standards.

5.1.2 Analysis of the Calibration Standards for Shimadzu TOC Analyzer

5.1.2.1 From the Shimadzu Main Menu select: File, New sample table.

5.1.2.2 Select the calcurve tab, drag calcurve and drop in first row of table.

5.1.2.3 Click on the sample carousel icon.

5.1.2.3.1 Enter the corresponding number in the Vial column for each sample in the vial setting table, starting with 1 and going in ascending order down the table. Place each sample in the appropriate spot in the carousel making sure to remove the plastic cap from the vials.

5.1.2.3.2 Replace the carousel and lid.

5.1.2.4 Select Save as using file format calmonthdayyear.t32, ex. Cal010116.t32.

5.1.2.5 Analyze the calibration standard(s) by selecting Start.

5.1.3 Applying the results of the analysis of the calibration standards to their calibration curve and subsequent samples.

5.1.3.1 Select Cal curve file by selecting file, open, sample table and current cal file ran.

5.1.3.2 Highlight row 1 and select the calibration curve properties button, indicated by the flask icon.

5.1.3.3 Select the graph tab to view cal. curve results, including r value and cal. curve ok confirmation.

5.1.3.4 The Shimadzu TOC Analyzer is now calibrated for TOC analysis. Calibration must be done weekly. It can be repeated throughout the week as needed.

6.0 Acceptance Criteria

6.1 The coefficient of linearity (r^2) must be ≥ 0.995 .

7.0 Definitions

7.1 Modes

There are three calibration modes.

NOTE: The TC-IC analysis mode uses the TC and IC calibration curves of data reduction.

7.1.1 TOC – Total Organic Carbon

7.1.2 TC – Total Carbon

7.1.3 IC – Inorganic Carbon

7.2 Ranges

There are five ranges of analysis for the TOC Analyzers. The theoretical maximum concentration of carbon for each range is the following:

7.2.1 Range 1: 2 - 100 ppb C

7.2.2 Range 2: 0.01 - 20 ppm C

7.2.3 Range 3: 20 - 200 ppm C

7.2.4 Range 4: 200 - 1000 ppm C

7.2.5 Range 5: 1000 - 10,000 ppm C

7.3 Calibration Curve

Computer files that stores all the information about a particular calibration data set including:

7.3.1	Calibration Curve ID	The name of the calibration curve.
7.3.2	Standard ID	The names of all of the standard solutions associated with this calibration curve ID.
7.3.3	Concentration (ppm C)	The standard solution concentration in ppm C (mg C/L).
7.3.4	Method ID	The method name and the variables associated with the analysis including the operating mode, range, injection volume, etc.
7.3.5	Expected µg C	The known mass of carbon in the analyzed calibration standard based on the input concentration (9.3.3) and the injection volume (9.3.4). It is plotted as the X axis on the calibration curve graph.
7.3.6	Raw Data	Integrator area counts before any calibration or blank values are applied (mV-sec.). It is plotted as the Y axis on the calibration curve graph.
7.3.7	Measured µg C	The amount of carbon measured in a standard after the calibration curve equation has been applied.
7.3.8	Date and Time	The time of each individual calibration standard analysis.

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| 7.3.9 | Created | The time when the standards were selected and applied to calculate the calibration factor, y intercept and r^2 values |
| 7.3.10 | Calibration Factor (m) | The slope of the calibration curve (raw data/ $\mu\text{g C}$ expected) |
| 7.3.11 | Y intercept (b) | The point at which the calibration curve crosses the Y axis. It is used as the calibration blank when calculating the result of the measured $\mu\text{g C}$ and the calibration verification samples. |
| 7.3.12 | r^2 | Square of the correlation coefficient (r) for the calibration curve. |

7.4 Reagent Blank

This is the system background due primarily to the carbon present in the reagents. There is a total of six reagent blanks, one for each type and volume of reagent processing. The persulfate reagent blank is called the TC blank and is applied to both the TC and TOC analysis. It has three ranges grouped 1, 2, and 3 - 5. The acid reagent is called the IC Blank. It is applied to the IC analysis and it too has three ranges grouped 1, 2, and 3 - 5. All reagent blanks are determined separately from the calibration routine and their values are stored and reported as raw data (mV-sec).

7.5 Active Calibration Curve

This is the calibration curve data that is applied to a sample analysis to calculate its carbon concentration. There is one active calibration curve for each mode and range.

7.6 Calibration and Method Verification Standards

These are standards that are used to check the performance of the system and its calibration. These standards are usually the same standards that were used to generate the calibration curve. These standards must be made from the same water source as the calibration standards.

8.0 References and Related Documents

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| 8.1 | SOP 22963 | <i>Operation of the Shimadzu TOC Analyzer</i> |
| 8.2 | SOP 22918 | <i>Glassware Cleaning for Trace TOC Analysis</i> |
| 8.3 | SOP 22919 | <i>Standard Preparation for TOC Analyzer</i> |
| 8.4 | SOP 22922 | <i>Preventative Maintenance for the TOC Analyzers</i> |